A COMPARATIVE STUDY OF VARIOUS FORMS OF ORAL IRON AND INTRAMUSCULAR IRON TREATMENT IN MODERATELY ANAEMIC PREGNANT WOMEN.

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BONAFIDE CERTIFICATE

This is to certify that the study entitled "**A Comparative Study of various Forms of Oral Iron and Intramuscular Iron Treatment in Moderately Anaemic Pregnant Women**" is the bonafide work done by **Dr.A.Shanthi,** at the Institute of Obstetrics and Gynaecology, Govt. Hospital for Women and Children attached to Madras Medical College, Chennai during the period of her Post Graduate study for MD Branch II Obstetrics and Gynaecology, from 2003 – 2006 under the guidance of **Prof.Dr.Cynthia Alexander, M.D. DGO., .**

This dissertation submitted to Dr.M.G.R. Medical University is in partial fulfillment of the University rules and regulations for the award of MD Degree in Obstetrics and Gynaecology.

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CONTENTS

INTRODUCTION

Anaemia in pregnancy exists world over but it is a very common problem in most of developing countries. Anaemia is major public health problem in economically disadvantaged segments of population in developing countries.

In country like India it is frequently severe and contributes to maternal mortality and reproductive healthy morbidity. It deserves more attention than what it is currently receiving. Recently lot of programmes have been focused on safe motherhood but maternal anaemia remains a problem of great concern.

Gender discrimination is another important factors in India and other Asian countries the girl child right from birth is denied of proper food and education which leads to iron deficiency anaemia during pregnancy.

Magnitude of the Problem

The world wide prevalence of anaemia in pregnant women is estimated at 51%, WHO states that 35% to 75% of pregnant women in developing countries and 18% of women in Industralised countries are anaemic.

In India, the incidence of anaemia among expectant mothers is alarmingly high with haemoglobin level less than 10 gm%, 15 to 30% of maternal deaths are due to anaemia.

In areas where malaria and hookworm infestation is endemic prevalence of anaemia is high as 90%. The incidence of anaemia in adolescent girls in slum areas estimated to 98% this adversely affect reproductive performance.

The prevalence of anaemia has come down due to fortification, prophylactic iron supplementation, better health care programme aimed at women and children.

AIM OF THE STUDY

To compare the efficacy of

Various Oral Iron

a. Ferrous sulphate

b. Sodium Feredetate (Sodium Iron EDTA)

c. Carbonyl iron

Parental Iron

a) Iron Dextran (Imferon)

In moderately anaemic pregnant women belonging to 24 to 32 weeks of gestational age.

NEED FOR THE STUDY

Anaemia is the most important complication in pregnancy in the developing countries not only because of its greatly increased incidence but also because of its severity ***(Agarwal A.K. et al, 1999)***.

Several studies reveal that socioeconomic cultural factors influence dietary inadequacy during pregnancy which is attributed to poor purchasing power, literacy, ignorance, regarding nutritive value of readily available cheaper food stuffs, cultural taboos, superstitions and large family ***(Menon Krishna et al, 1995, Ruth Bannet and Brown linding 1993, Naik D, jayashree 1992)***. Nutritional iron deficiency anaemia is a serious problem in pregnancy which affects 90% pregnant women.

Severe forms of anaemia in the third trimester of pregnancy are invariably associated with cardiac failure. Highest maternal mortality rate in developing countries is due to severe anaemia, contributing to 20% death both directly and indirectly. It is also responsible for incidence of premature and low birth weight babies thus increasing perinatal and infant mortality and morbidity.

According to ***Hassan Masood 1991***, anaemia is prevalent among 50% - 90% pregnant women especially in India, which is the number one killer. Despite considerable improvement and awareness in antenatal care in developing countries and inspite of national anaemia propylaxis programme in

India anaemia remains a problem of great concern with regard to maternal morbidity, mortality and adverse outcome ***(Singh Kishore C et al, 1995)***.

Due to above stated reasons this study emphasis on regular antenatal check up, to screen for anaemia during every check up detect it earlier so that it can be treated adequately before the mother reaches term gestation. The goal of the treatment is to increase the haemoglobin status as rapidly as possible.

REVIEW OF LITERATURE

Definition of Anaemia

Anaemia is a condition of low circulating haemoglobin (Hb) in which the Hb concentration has fallen below a threshold lying at two standard deviations all below the median of healthy population of the same age, sex and stage of pregnancy.

WHO definition for diagnosis of anaemia in pregnancy is a Hb concentration of less than 11gm/dl and a haematocrit of less than 33, although CDC (Centres for Disease Control USA) proposes a cut off point of 10.5gm/dl during the second trimester.

Severity of Anaemia

The Indian Council of Medical research uses four categories of anaemia depending upon the haemoglobin levels in their study are

S.No.	Category	Hb Status g/dl
1.	Mild	10 – 10.9
2.	Moderate	7 – 10
3.	Severe	< 7
4.	Very Severe (Decompensated)	< 4

Causes of Anaemia

I. Physiological anaemia or hydremia of pregnancy

II. Pathological Anaemia

a. Nutritional – Iron, folic acid, Vit B12, Protein

b. Hemarrhagic

Acute -	Following bleeding in early pregnancy,. H/o. abortion or vesicularmole previously
Chronic-	Hookworm infestation, bleeding haemarhoids, ulcerative colitis, malignancies

c. Haemolytic

Familial	Haemoglobinopathies
Acquired	Malaria, Severe Infection

d. Bone Marrow insufficiency

Hypoplasia or aplasia due to radiation, drugs (aspirin, indomethacin)

CAUSES OF NUTRITIONAL ANAEMIA DURING PREGNANCY

Nutritional anaemia is believed to be the most widespread nutritional disorders in the world. It essentially affects people in developing countries. According to WHO 500 million to 1 billion individuals representing 15 to 20 percent of worlds population is presently affected by this condition.

According to WHO definition, the "nutritional anaemia" encompasses all pathological conditions in which the blood haemoglobin concentration drops to an abnormally low level owing to a deficiency in one or several essential nutrients, regardless of the cause of this deficiency.

The etiology of nutritional deficiency of iron in developing countries is multifactorial. The causes include nutritional deficiency of iron, folate and vitamin B_{12}, secondary effects of infections and parasitic infestation. An imbalance occur as a result of low nutrient intake, poor absorbtion, increased demand of nutrients during pregnancy, increased nutrient loss due to repeated pregnancies, short birthinterval and menstruation. Dietary short coming are often associated with low socio economic status and related to cooking and dietary habits, local food taboons, ignorance, illiteracy and lack of knowledge regarding nutrition ***(Van De, 1998)***.

The etiological factors of nutritional anaemia in pregnancy.

a) Dietary factors
b) Increased demand during pregnancy
c) Maternal causes
d) Sociocultural factors
e) Infections and Infestation

a) Dietary factors

Inadequate intake of food

a. Low nutrient intake is the commonest cause of nutritional anaemia
b. Main nutrients involved in synthesis of haemoglobin are iron, folic acid, Vit B_{12} and deficiency of these cause anaemia

Low iron absorption

Poor absorption and utilization of iron in the body is one of the causes of iron deficiency anaemia during pregnancy.

Factors decrease Iron absorption

a. Phytates
b. Calcium
c. Tannins
d. Tea and coffee
e. Herbal drinks
f. Fortified iron supplements

b) Increased Demand during pregnancy

Increased demand for nutrients is one of the major causes of nutritional anaemia during pregnancy ***(Bucksher et al., 1996)***. The increased blood volume during pregnancy results in dilution of red cells and a reduction in haemoglobin concentration. This dilutional anaemia is potentially accentuated by the increased demands of iron and folic acid leading to anaemia.

Poor absorption of iron occurs due to the fact that Indian diet is predominantly cereal based.

Though Indian diet has adequate iron content 20 – 25mg/day several factors inhibits absorption, the most important being the phytate from the cereals. Deficiency of ascorbic acid and calcium inhibits iron absorbtion.

Factors Affecting Absorption

Factors increase absorption

a. Hydrochloric acid by favouring dissolution and reduction of ferric iron.
b. Reducing substance like ascorbic acid, aminoacids containing sulphydryl radical, these reduce ferric to ferrous iron.
c. Meat contain organic iron and increased HCL secretion
d. Food containing low phosphorus diet.

There is increased demand for iron as it is essential for the synthesis of increased haemoglobin required for the greater maternal blood as well as for the storage of iron in the fetus. When the mother does not meet this demand,

she may develop features of iron deficiency anaemia. It is needed not only to compensate the usual losses in urine, faeces, cutaneous desquamation (around 0.5 – 1 mg per day) but also to cover the various pregnancy related expenditure. Total 1000 mg of iron is required. This represents an extremely large amount to meet, if not looked after it can result in iron deficiency anaemia ***(Hercubury 1991)***.

The requirements of iron is not confined only to those aspects of the fetus but also the placenta, the enlarged uterus and for increased volume that occurs during pregnancy.

The estimates of iron requirements are

Foetus	:	400 mg
Placenta	:	100 mg
Uterus	:	50 mg
Hb	:	320mg
Total	:	870 mg

c. **Maternal Causes**

Depletion of nutrients occur in maternal body due to various reasons. The women may have entered pregnancy with compromised or absent iron stores. When further iron depletion occurs with advancing gestation anaemia results ***(Zuspan and Huilligun, 1994)***.

In tropics frequent pregnancies are the common cause of iron and folic acid deficiency anaemia among pregnant mother ***(Buckshee et al 1996)***. Iron

depletion occurs due to uncompensated menstrual loses and chronic blood loss due to repeated pregnancies

Grand multipara is considered as one of the cause contributing to nutritional anaemia during pregnancy as it is associated with increased incidence of disorders like hypertension, antepartum haemorrhage and others. The co-existing pathological condition like APH, PPH, abortions lead to iron deficiency results in iron deficiency anaemia ***(Buckshae et al, 1996) (Modak et al 1994)***.

There are maternal causes which lead to nutritional anaemia during pregnancy. These are

a. Anaemia in multigravida or multipara is mainly due to blood loss in previous deliveries or pregnancies.
b. Repeated abortions, APH, PPH
c. Extra demand for iron, folic acid in multiple pregnancy
d. Short interval between pregnancies
    i. Less storage of iron in the mothers body since it is already utilized by the previous pregnancy.
    ii. There is no time for storage of iron in the body for the next pregnancy

d) Socio Cultural Factors

i. ***Poor Socioeconomic Status***

As the women continue to be a socially disadvantaged group, their poor status affects nutrition.

ii. Cultural belief, Cooking and Eating habits food taboos

Cultural practices play an important role in cause of nutritional anaemia in pregnancy. Because of taboos the pregnant mothers avoid meat, fish, egg, jaggery, curds, milk and leafy vegetables. Over cooking of food, washing of vegetables several time may lead to loss of nutrients in the food. This may also lead to nutritional anaemia in pregnancy ***(Vande 1998).***

e. Infection and Infestation

i. Hookworm infestation

Hookworm infestation is considered as one of the cause of nutritional anaemia among the pregnant women ***(Agarwal et al, 1999)***.

Infestation with hookworm, roundworm and whipworm cause or aggravate iron deficiency anaemia ***(Sephension 1994)***.

Hookworm infestation also leads to the deficiency of folic acid in pregnant women (Buckshee et al 1996).

ii. Malaria

Plasmodium falciparam cause profound anaemia during an acute infection among pregnant women ***(Agarwal et al, 1999)***.

Erythropoiesis

In human embryo haemopoiesis is first evident in yolk sac at 2 months, liver at 3rd month and to some extent spleen between 3rd and 6th month. Bone marrow activity begins by 4th and 6th month, it completely take over the process of haemopoiesis.

At birth bones are filled with red marrow, by 7 years marrow in long bones is less active, by age of 10 to 14 years fatty marrow extends proximally and 18 years normal adult distribution of marrow is in the skull, axial skeleton, pelvis shoulder, sternum ribs and with extension of proximal ends of long bones.

Stages of Erythropoiesis

i. Basophyllic proerythroblast
ii. Early normoblast
iii. Intermediatenormoblast
iv. Late normoblast
v. Reticulocyte
vi. Erythrocyte

Kinetics of Erythropoiesis

The time taken for erythropoiesis in human beings is about 7 days. The first 5 days are occupied by division and maturation upto non nucleated reticulocytes in the marrow and the reticulocytes normally mature for another 24 hours in the peripheral blood and spleen, after which it circulate for 120

days. Since about 1% of circulating erythrocytes are destroyed each day, same number are formed and released. Factors regulating erythropoiesis

a) Androgen stimulates, esterogen suppresses erythropoiesis

b) Thyroidhormone and adrenocrotical steroids stimulates erythropoiesis

c) Nutritional factors like proteins, Vit B_{12}, folic acid, Vit B_6, riboflavin, pantothenic acid, nicotinic acid, ascorbic acid, Vit E, mineral like copper cobalt, zinc and iron.

IRON COMPARTMENTS IN HUMAN

Haemoglobin : 1ml of packed RBC contain 1mg of iron and size of this compartment changes in anaemia

Storage : Ferritin and Haemosiderin

Ferritin : It is a water insoluble complex of ferrtic hydroxide and protein apoferritin. Uptake and release of iron by ferritin is very rapid. Ferritin occurs in all cells of the body. Its concentration correlates with iron store. Hamosiderin water soluable compound found predominantly in cells of monocytes macrophage system

Myoglobin : Present in all skeletal and cardiac muscles cells

Transport Iron :

Active transport process explained by "*Mucosal Block Theory*". According to this theory ferrous form absorbed in small intestine converted to

ferric form in the intestinal villi this combine with apoferritin in the villous epithelial cell to form ferritin.

Absorption of iron is controlled by the availability of apoferritin. If this is fully saturated no more iron is absorbed, and this protects from excessive absorption in anaemia. In anaemia excess ferritin is brokendown make more apoferritin available and thereby augments iron absorption. This intracellular ferritin is eventually excreted following desquamation of epithelial cells of intestine.

IRON TRANSPORT AND UTILIZATION

Iron after absorption circulate in the blood bounded to a β globulin transferin which is normally 1/3 saturated with iron. Normal iron varies from 66 – 140 microgram / 100 mg plasma.

Physiological changes in Haemoglobin during pregnancy

In pregnancy there is progressive increase in circulating blood volume due to increase in plasma and RBC volume

Increase blood volume ranges from 30 – 70% of the non pregnant level.

Increased blood volume due to maternal size, level of placental and extraplacental hormones and erythropoietin, influence the increase in blood volume.

The increase in plasma volume is 40 – 50%.

The increase in RBC volume is 20%.

Anaemia during pregnancy is a consequence primarily of expansion of plasma volume without normal expansion of maternal haemoglobin.

This is called physiological anaemia because

i. It begins in I trimester when the iron needs are fullymet.

ii. Occurs in well nourished women

Physiological Anaemia Occurs Because

i. Increase in plasma volume and RBC volume occur at different periods of pregnancy.

ii. Plasma volume begins to rise at 6 – 8 weeks of pregnancy reaches peaks at about 32 weeks after it plateaus

iii. The rise in RBC volume begins at 20 weeks and continue till term. There is trend for mean Hb fall in the first and second trimester and little rise later in the third trimester ***(Peckand Ariyas 1979)***.

Haematological Parameters

Normal blood values in non pregnant status

RBC - 4.8 – 6 million / cumm

Hb - 12 – 14 gm / dl

PCV - 40 – 45%

Life span of RBC is 110 – 120 days

Normal blood values during pregnancy

RBC - 4.5 million / cumm

Hb	-	12 – 13.4 gm/dl
PCV	-	37 – 42%
MCV	-	80 – 90 cubic microns
MCHC	-	28 – 34%
MCH	-	27 – 32 Picogram
Colourindex	-	0.9 - 1

$$\text{Mean corpuscular Hb MCH} = \frac{\text{Hb in gm per 1000ml blood}}{\text{RBC in million /cumm}}$$

Normal = 29.5 pico gm

$$\text{Mean corpuscular Volume MCV} = \frac{\text{Volumes of packed cell per 1000ml}}{\text{RBC in million /cumm}}$$

Normal = 68 cubic microns

$$\text{Mean corpuscular Hb concentration MCHC} = \frac{\text{Hb in gm per 100 ml}}{\text{Volume of packed cell per 100 ml}} \times 100$$

Normal = 34 percent

$$\text{Colour index} = \frac{\text{Hb (percentage of normal)}}{\text{RBC (percentage of normal)}}$$

Normal = 0.9 - 1

SYMPTOMS AND SIGNS:

Symptoms: complaints of fatigue, poor tolerance of exertion, weakness and lassitude. Other features are anorexia and indigestion; palpitation caused by ectopic beats, dyspnoea, giddiness, and swelling of legs.

Signs:

Pallor:

Pallor of varying degree is evident. The colour of the lips, tongue, innerside of the lower eyelid, palms, and sole are pale. If the colour of palmar creases are as pale as the surrounding skin the haemoglobin is usually less than 7 gm/dl.

Nailbed should be examined for pallor, the rapidity of capillary refill is an indicator of integrity of the cardiovascular system.

Koilonychia:

Koilonychia is strongly suggestive of Iron deficiency and is demonstrated as spoon shaped nails.

Glossitis:

Ulceration in the mouth and tongue. The painful dry tongue of glossitis is helpful in diagnosing Vit B12 deficiency anaemia. Angular stomatitis is also associated.

Oedema legs:

This is due to hypoproteinemia.

Cardiovascular changes:

Cardiovascular signs reflect decompensation a soft systolic murmur may be heard in mitral area due to mitral incompetence. Crepitation may be heard at the base of lungs due to congestion.

Investigation:

1. Maternal condition.
2. Fetal condition.

Maternal condition: a) Type and degree of severity. The investigations include,

a) Hb%
b) RBC count.
c) PCV.
d) Blood indices.

MCV – Normal 78 – 92 cu micron.

< 78 microcytic suggest iron def.

> 92 macrocytic follate def.

MCH – Normal 28 – 33 pgm.

↓ in iron def anaemia.

MCHC – 33 – 36%

↓ in iron def anaemia.

Peripheral smear:

This simple investigation often throws light on the etiology.

a) Microcytic hypochromic cells.

b) Macrocytic hyperchromic cells.

c) Normocytic normochromic cells.

1) Microcytic hypochromic cells are seen in,

a) Iron deficiency.

b) Thalessemia.

c) Sideroblastic anaemia.

d) Anaemia of chronic disease.

e) Lead poisoning.

f) Copper poisoning.

2) Macrocytic hyperchromic cells:

a) follate/vit B12 deficiency.

3) Normocytic normochromic.

b) other causes or early nutritional deficiency.

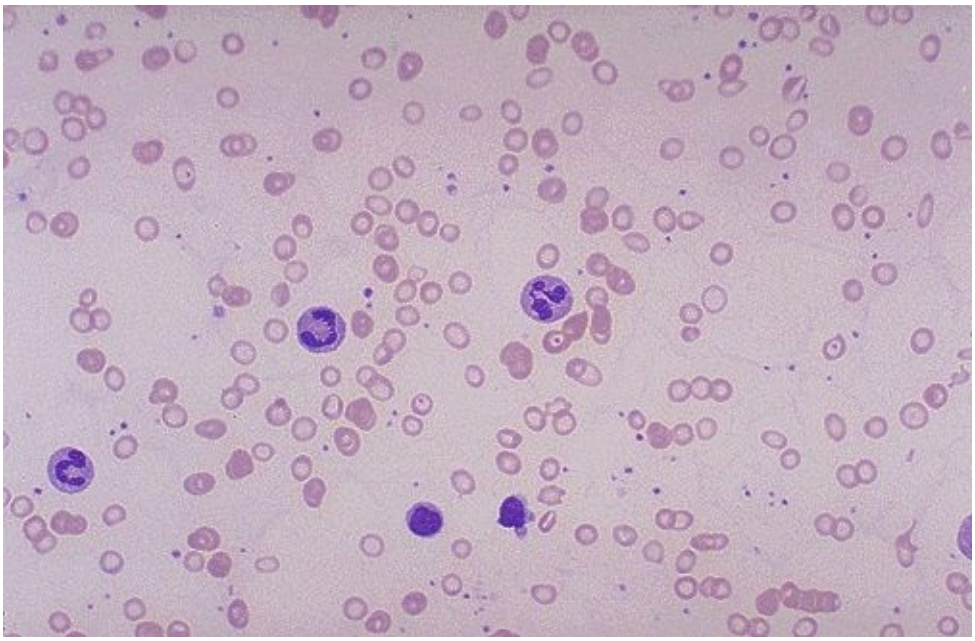
4) Schisto/aniso and poikilocytes:

Haemolytic anaemia.

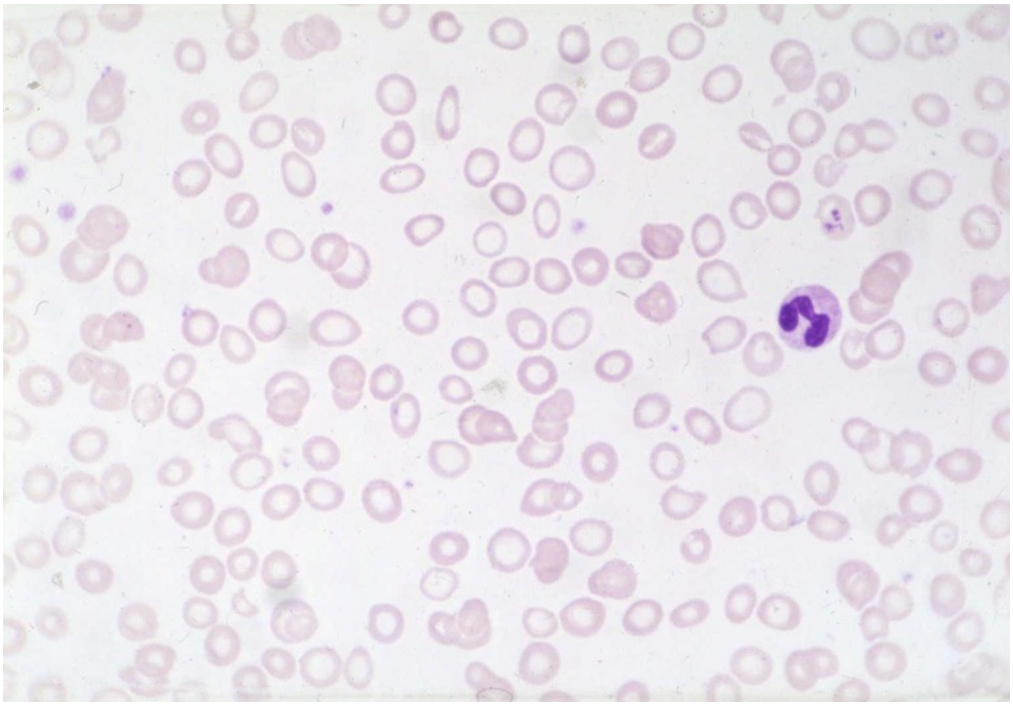
5) Target cells:

Thalessemia.

MICROCYTIC HYPOCHROMIC BLOOD PICTURE



NORMOCYTIC HYPOCHROMIC



6) Sickle cells:

Sickle cell anaemia.

7) Hypersegmented polymorphs:

Seen in megaloblastic anaemia.

8) Platelet:

May be decreased.

9) Parasites:

Such as malaria and leishmania may be seen.

B. Investigation for etiology.

Urine examination:

Urine albumin, sugar and deposits, and urine culture and sensitivity to rule out infection.

Stool examination:

- Parasites (ova of hookworm).
- Occult blood loss.

C. SPECIAL INVESTIGATIONS

I. **Ferrokinetics:**

These are tests that confirm the diagnosis and severity of iron deficiency anaemia.

a) Serum ferritin.

   Abnormal when < 15 ngm/ml.

b) Serum transferrin iron binding capacity.

   Normal 300 – 360 g/ml. Value increases with severity of anaemia.

c) Serum iron.

   Normal 65-165 gm/dl. It is ↓ in iron def anaemia.

d) Percentage saturation of transferrin.

   Normal 35 – 50%. This value is ↓ 15% in iron def anaemia.

e) RBC protoporphyrin – 30 gm/dl. This value is found doubled or tribled.

f) Total iron binding capacity.

   Increased up to 550 gm/dl or even more.

II. **Investigations Of Megaloblastic Anaemia**

MCV 110 – 140 cu/microns.

MCH 33- 36 pg.

Serum follate < 3 gm/litre.

RBC follate < 80 gm/litre.

Serum vit B12.

Peripheral smear macrocytic and hypersegmented.

Serum B12.

Buffy coat.

FIGLU test.

III. **Investigation in hemolytic anaemia.**

a) Osmotic fragility.

b) Coombs test.

c) Haemoglobin electrophoresis.

IV. **Tests to ensure therapy.**

1. Reticulocyte count – increases.

2. Haemoglobin - increases.

3. Peripheral smear - ↓ in abnormal cell type.

V. **Screening test.**

Haemoglobin must be determined by Sahlis haemoglobin method at the first antenatal visit. It should be repeated in all antenatal visit ideally at 32 weeks gestation when their haemodilution is at its peak.

Effects of nutritional anaemia during pregnancy.

Nutritional anaemia among pregnant women is associated with adverse consequences to both the mother and the foetus. These adverse effects vary upon the severity of anaemia and presence of other obstetric or systemic problems in anaemic women (Lewis and Chamberlin 1999).

Effect on the mother:

1. Iron deficiency anaemia among pregnant women leads to diminished work capacity, physical performance, and neurological dysfunction.
2. More prone for infections.
3. Antepartum and postpartum haemorrhage are more common in anaemic mothers.
4. Antenatal mothers go for cardiac failure during labour.
5. Puerperal pyrexia.
6. Puerperal sepsis.
7. Subinvolution.
8. Lactation failure.
9. Episiotomy wound gaping and abdominal wound gaping.
10. Abortion.
11. Folate deficiency leads to PIH, abruptio placentae.
12. Maternal and perinatal morbidity and mortality increases

Effect on fetus

Nutritional anaemia due to iron and folic acid deficiency is the cause of abortion, premature birth, low birth weight, foetal wastage like abortion, intrauterine death, and stillbirth occur in about 20% of the conception due to anaemia (Sethi et al. 1991) (Kelton et; 1988) IUGR, impaired learning ability in children.

- Folic acid deficiency has been implicated as a cause of foetal malformation especially neural tube defects.
- Maternal iron deficiency anaemia leads to lower iron rescue in infancy.
- Severe nutritional anaemia among pregnant mother leads to increased risk of intrauterine hypoxia, higher perinatal and neonatal mortality and morbidity.

PREVENTION OF IRON DEFICIENCY ANAEMIA

Prophylaxis of non pregnant women:

Girls in India are deprived of good diet. As most women start their pregnancy with anaemia or low iron stores, prevention should start even before pregnancy. The women of child bearing age should receive 60 mg of iron daily for 2 – 4 months along with follic acid to prevent neural tube defects.

Iron supplementation during pregnancy

The ministry of health government of India now recommended intake of 100 mg of elemental iron 500 µgm folic acid in the second half of pregnancy for a period of at least 100 days.

Treatment of hookworm infestation:

Single dose albendazole 400 mg or mebendazole 100 mg twice daily for 3 days with iron supplementation should be given to all anaemic pregnant women.

4. Improvement of dietary habits

Pregnant woman should eat foods rich in iron jaggery, green leafy vegetables like spinach, mustard leaves, turnip green, cereals, sprouted pulses. Avoid tea and coffee intake, too much cooking should be avoided.

5. proper antenatal care.

a) antenatal mothers should have regular antenatal checkup which should begin in first trimester of pregnancy.

b) HB% estimation should be done during every A.N visit.

c) Iron and folic acid should be consumed daily.

d) Proper treatment of infection.

6. Health education

    1. By limiting number of children 1 to 2.
    2. The ideal interval between 2 successive pregnancy should be 3 year.
    3. Ideal age for child bearing is 20 – 25 yrs.

TREATMENT OF IRON DEFICIENCY ANAEMIA

Oral iron therapy

If the women presents with in mid trimester or early third trimester with anaemia oral iron is started. Plenty of iron preparation are available each with own advantages and disadvantages.

DOSAGE:

Ferrous sulphate tablets are used in all government hospital for oral treatment of anaemia. For treatment more than 180 mg of elemental iron per day is required. Two tablets of ferrous sulphate each containing 100mg of elemental iron per day is required for treatment.

Side effect:

Upto 10% of women may have side effects with oral iron in the form of gastrointestinal symptoms such as nausea, vomiting, constipation, abdominal cramping and diarrhea which are dose related. Side effects can be minimized by advising to take the tablet with food.

Response to treatment:

The patient's response to 180 mg elemental iron per day is fast with significant increase in HB from 0.3 to 1 gm per week. Reticulocytosis occur within 5 – 10 days of treatment.

Duration of treatment:

Treatment should be continued until the blood parameter become normal after which a maintenance dose of 1 tablet per day should be continued for at least 3 months after delivery.

Disadvantage of oral iron treatment:

a) Intolerance to medication.

b) Noncompliance.

c) Unpredictable absorption.

d) Haemoglobin concentration restored with therapeutic dose but replenishing iron stores required treatment for longer periods.

If there is no significant clinical or haematological improvement within 8 weeks diagnostic reevaluation is needed. Reasons for failure to oral therapy involve inaccurate diagnosis of non iron microcytic anaemia such as thalessemia, pyridoxine deficiency, lead poisoning, continuous loss of blood through hookworm infestation, Co-existing infection, faulty iron absorption, concominant folate deficiency.

a. FERROUS SULPHATE

Ferrous sulphate tablets available in Government Hospital contains 100mg of elemental iron.

b. **CARBONYL IRON**

Carbonyl iron is a pure form of elemental iron that contains 98% mineral iron which is a small particle preparation of highly purified metallic iron. It is a form of elemental iron produced by a chemical carbonyl decomposition process. Carbonyl describes the process of manufacture of iron particles from iron penta carbonyl gas.

Bioavailability:

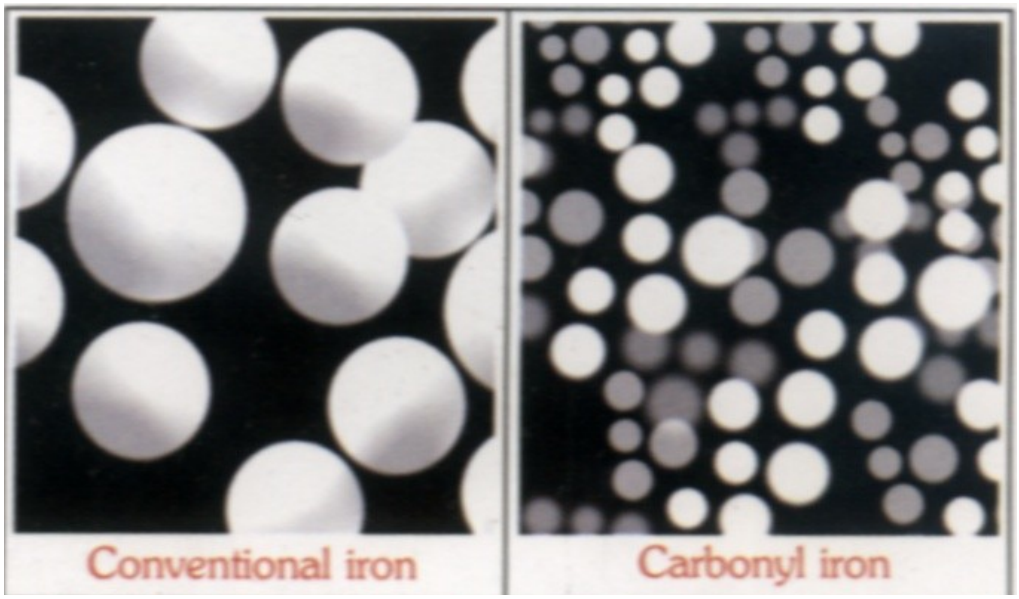
Carbonyl particles are small < 5μ and have large surface areas which results in improved bioavailability.

Carbonyl iron has been shown to be well absorbed and utilized in Hb synthesis. Its advantage includes environmental stability.

Safety Profile:

Carbonyl iron is much less toxic than ionized forms of iron. In humans lethal dose of ferrous sulphate is 200 mg/kg. In recent study no serious toxicity was reported in all patients with mean carbonyl iron ingestion of 11.2 mg/kg.

COMPARISON BETWEEN CONVENTIONAL IRON AND CARBONYL IRON PARTICLES



Side effects:

Carbonyl iron does not have many of the side effects associated with other iron products particularly ferrous sulphate such as GI irritation, nausea, constipation or diarrhea. There was no evidence of haematologic, hepatic, or renal toxicity.

Advantages of carbonyl iron:

i) It is 98% pure form of iron. The percentage of elemental iron in carbonyl iron is 98%.

ii) Unlike other preparation it is inert and incapable of reacting with chelators of iron such as transferrin and desferraxamine.

iii) It leads to a rapid rise in haemoglobin.

iv) It has a wide margin of safety.

v) It is free from gastric side effect.

vi) It is safest in pregnancy.

SODIUM FEREDETATE:

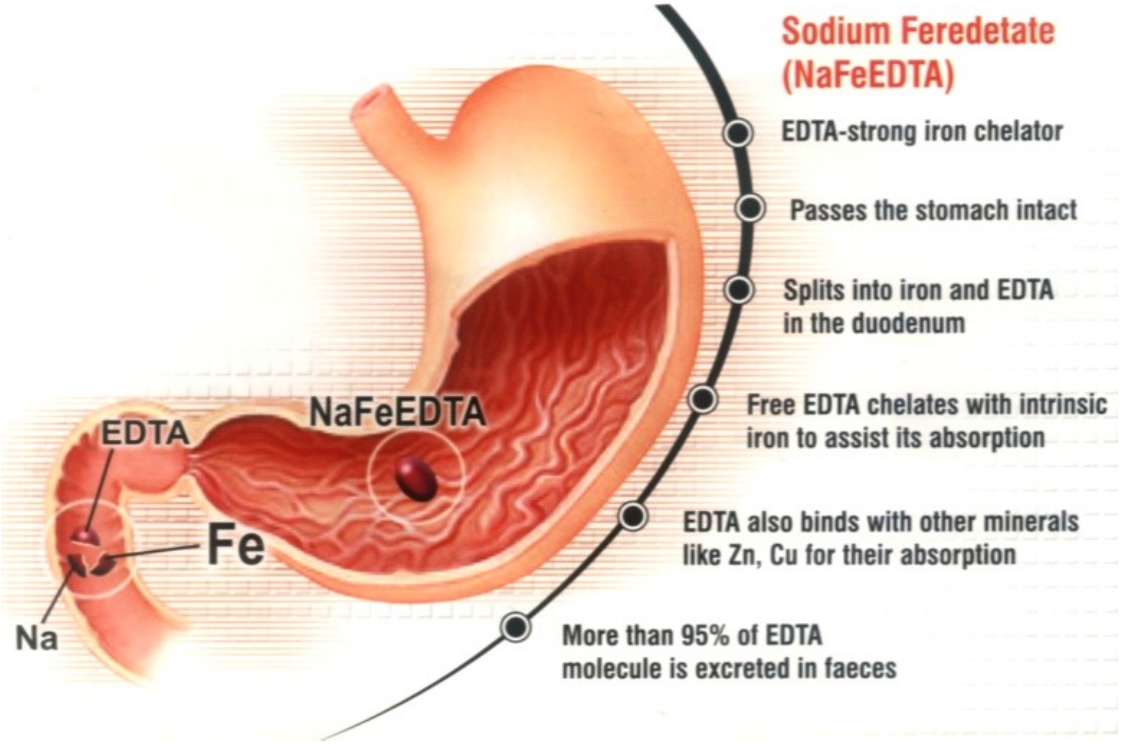
Synonyms:

Sodium iron EDTA, sodium feredetate, edetic acid, sodium iron salt.

CHEMICAL NAMES:

Sodium iron III ethylene diamine tetraacetate.

ABSORBTION OF SODIUM FEREDETATE



CHEMICAL FORMULA:

$C_{10}H_{12}FeN_2Nao_8$:3 H_2O.

MECHANISMS OF ACTION:

Sodium Feredetate is stable in acidic environment and hence no dissociation of sodium Feredetate complex takes place in stomach. It is only when it enters the duodenum that dissociates into EDTA and iron. Iron absorption begins where iron is made available to the mucosal cells. The free EDTA then acts as a shuttle and picks up more iron, copper, zinc from the food and delivers into mucosal cells. Absorption of iron is not inhibited by other inhibitory ligands.

Excretion of EDTA:

95% of EDTA molecule is excreted in faeces and 5% in urine within 24 hours.

PARENTERAL IRON

It is indicated in patients who cannot absorb iron, noncompliant or develop serious side effects with oral iron which cannot be corrected by simple means.

Iron deficit is calculated,

(normal Hb – patients Hb) x wt in Kg x 2.21 + 1000.

The parenteral iron is available as Iron dextran (Imferan) which can be given intramuscularly or intravenously. Iron sorbital citrate which can be only given intramuscularly.

IRON DEXTRAN INJECTION:

Iron dextran injection is a collidal solution of ferric oxyhydroxide complexed with polymerized dextran that contain 50 mg/ml of elemental iron. It can be administered by either intravenous or intramuscular injection. When given by deep intramuscular injection it is gradually mobilised via the lymphatics and transported to reticuloendothelial cells. Iron is released from the dextran complex.

INTRAMUSCULAR IRON:

Oral iron should be stopped before giving intramuscular iron as it is associated with toxic reaction initially test dose of 1 ml of iron dextran is given deep intramuscularly if there is no reaction the injections are given daily or on alternative days in doses of 2 ml intramuscularly by using Z technique in the outer quadrant of buttock. Z technique involves pulling the skin and subcutaneous tissues to one side before inserting the needle.

Advantages:

1. The main advantage is certainty of its administration to correct the Hb deficit and build up the iron stores.

Disadvantages:

1. Pain, skin discolouration, and abscess formation, reaction in the form of nausea, vomiting, headache, fever, lymphadenopathy, allergic reaction and rarely anaphylaxis.

Intravenous infusions

Total iron requirement is calculated using the above formula. Intravenous infusion should be given in the hospital setting by doctors to patients with no allergy to test dose. Injection epinephrine, hydrocortisone, oxygen should be available in the event of anaphylactic reaction. Iron dextran is diluted in normal saline or 5% dextrose and given slowly initially. If there is no reaction, it can be given faster. If the calculated dose is more than 250 mg, it should be given 2 doses on two consecutive doses. One should look for any reaction in the form of chest pain, rigor, chills, fall in blood pressure, dyspnoea, haemolysis, and anaphylactic reaction. For any such reaction, infusion should be stopped and antihistamine, corticoids, and epinephrine given.

Blood Transfusion

Blood transfusion is required in patients with severe anaemia beyond 36 wks, associated infection, to replenish blood loss due to antepartum or postpartum haemorrhage and in patients not responding to oral or parenteral iron therapy. Packed cells are preferred for transfusion.

Blood transfusion may cause preterm labour, precipitated labour, and overloading of heart. Exchange transfusion is used very rarely in some centres for severe anaemia.

MANAGEMENT OF LABOUR IN ANAEMIC PATIENTS:

First stage:

Patient should be in a comfortable position. Sedation and pain relief should be given. Oxygen should be kept ready and is given in dyspnoea. In case of preterm labour, betamimitics and steroids should be given with caution to avoid risk of pulmonary oedema. Digitalization may be required in cardiac failure due to anaemia. The aim is to deliver vaginally.

Second stage:

The second stage is very stressful as the patients may go in for cardiac failure. Prolongation of second stage can be curtailed by forceps.

Third Stage:

Third stage must be energetically treated as these patients tolerate bleeding very poorly. Prophylactic methergin should be given. Oxytocin 20 U infusion slowly given. Episiotomies wound should be sutured faster.

Puerperium:

During puerperium mother should have adequate rest. Iron and folate therapy should be continued for at least 3 months. Any infection must be energetically treated. The anaemic patient must use an effective method of contraception and should not conceive for at least 2 years until the iron stores are replenished. Sterilisation is preferred if the family is completed.

Several studies were done to compare the efficacy of different treatment using oral and parentral iron.

"A prospective partially randomized study of pregnancy outcomes and haemtologic responses to oral and intramuscular iron treatment in moderately anaemic pregnant women". This was done in Moulana Azad Medical College, New Delhi, Conducted by Jaib Sharma, Sandya Jain, Venkatesan Mallika, Tejinder Singh, Ashok Kumar. This study compared the safety and efficacy in treating pregnancy anemia with intramuscular iron and ferrous sulphate. Changes in haemoglobin iron indicators, pregnancy outcomes and birth weight were compared between the 2 groups. The result obtained were serum ferritin concentration rise after parental iron treatment better than oral ferrous sulphate group.

Similar other studies :

1. "A novel rigime of intramuscular iron therapy" Srivastave Aarti, Tanden Prabha, Darvineta conductdd in ICMR Department of Obstetric and Gynaecology KGMU Lucknow. In this study 200 mg iron dextrin was given to mildly anaemic pregnant women as deep intramuscular injection for 5 days. Then mean rise in haemoglobin after 4 weeks was significant than oral ferrous sulphate.
2. Iron dextron in the treatment of iron deficiency anaemia of pregnancy stein ML, Gunston KD, Mey RM.
3. New Schedule of intramuscular iron administration for pregnant women Mahale AR, Shah SH.

Bioavailabilty of carbonyl iron a randomized double blind study Devasthali SD, Gordeuk VR, Brittenham GM, Bravo JR, Compared ferrous

sulphate with carbonyl iron in blood donors. The study showed bio availability of Carbonyl iron was better with Carbonyl iron.

High dose carbonyl iron for iron deficiency anemia a randomized double blind trial Gordeuk, Brittenham. The study concluded that high dose carbonyl iron was well tolerated than standard ferrous sulphate in higher dosage.

In food and nutrition research institute Department of Science and technology Manila, study was conducted by Trinidad TP, Valdez, regarding iron absorption from Iron fortified rice with different forms of iron fortificant, ferrous sulphate, ferrous EDTA, ferrous fumarate and ferrous Bisglycinate and the study concluded NaFe EDTA showed a better iron absorbtion.

Similar other studies

a. Effectiveness of NaFe EDTA – fortified soy sause in controlling iron deficiency in China by Chen J Zhao

Regular consumption of NaFe EDTA fortified fish sauce improves iron status and reduced the prevalence of anaemia in Vietnamese common They PV, Berger J, Davidson L.

MATERIALS AND METHODS

The study was conducted from February 2005 – February 2006 in Hospital for Women and Children Egmore (Institute of Obstetrics and Gynaecology) attached to Madras Medical College.

The antenatal women attending the antenatal OP are screened for Haemoglobin status. Those antenatal women of gestational age 24 – 32 weeks with hemoglobin between 8- 9.5gm% were selected 200 of those women was selected.

Exclusion criteria :

i. Women with diabetes, hypertension significant medical complication such as heart disease or any other systemic disease are excluded

ii. Gastro intestinal bleeding or malabsorbtion, Bleeding piles and bleeding from any other site is excluded.

iii. Multiple pregnancy

iv. Previous blood transfusion

v. Recent administration of iron for treatment of anaemia

Investigation performed were

a) Haemoglobin estimation

b) Peripheral smear study

Determination of Haemoglobin level :

Sahlis Haemoglobino meter

0.1N HCl was sucked by an ordinary pipette was poured into the graduated dilution tube upto 20 mark on percentage side or 2 mark on gram percentage side. Blood was sucked by the haemoglobin pipette transfused to dilution tube containing. 0.1N HCl stirred with stirrer. The dilution tube was allowed to stand for 5 minutes. The colour of the dilution tube was compared with that of the standard in day light. Distilled water is added further to equal the colour of the mixture with standard, distilled water is added in succession of 3 – 4 drops and each time it was mixed with the stirrer. Towards the final point the number of drops may be reduced to get the right point accurately. The scale was read which gave the hamoglobin as gram %.

Peripheral smear :

Blood smear was stained with leishman stain morphology of redcells was noted.

A written informed consent was obtained from the patient eligible to participate in the study.

The patients eligible to participate were randomized to one of the four treatment groups. Randomization was done in such a way body mass index, gestational age, haemoglobin status initially was equal in all four treatment group.

After selection the patients were subjected to detailed history and physical examinations and the findings were noted. Initial haemoglobin status and peripheral smear was noted.

All the women in the study group was given T – albendazole 400mg single dose.

4 groups of treatment groups are

Group A Ferrous Sulphate Group

50 of the selected group received ferrous sulphate 100mg of elemental iron with folic acid 0.5mg tablet one tablet twice a day

Group B Sodium Feredetate Group

50 of the selected group received sodium feredetate 100 mg elemental iron with folic acid 0.5 mg twice a day

Group C Carbonyl Iron

50 of the selected group received carbonyl iron 100mg elemental iron with folic acid 0.5mg one tablet twice a day.

Group D Imferon Group

Total iron requirement = (normal Hb – patient's Hb) x wt in Kg x 2.21 + 1000

Normal Hb = 11gm% as per WHO standard

Iron requirements was calculated, iron dextran injection was given according to requirement. 100mg per day daily till the requirement is met after test dose. The patients were advised to take follic acid tablet 5mg twice weekly.

Patients were evaluated apart from baseline at 2 week interval adverse effect if any reported were noted, whether the patient could tolerate oral iron is noted, and vital like blood pressure and pulse rate noted. The patient should

bring back the empty packs of tablets and there were enquired about the colour of the stool.

At the end of 4 weeks repeat haemoglobin estimation was done. The results and data was analysed with statistical test.

If the haemoglobin at the end of 4 weeks was 11gm% then ferrous sulphate 100mg of elemental iron i.e., 1 tablet is continued till 3 months after delivery. If the Hb is less than 11gm% ferrous sulphate 100mg of elemental iron one tablet twice a day is given till 11gm% is reached.

OBSERVATION AND RESULTS

Table -1

GROUP A FERROUS SULPHATE

S.No.	Initial Hb% gm%	No. of Patients	Percentage
1.	8 – 9	23	46%
2.	9 – 9.5	27	54%

46% of the patient had initial Hb 8 – 9 gm%

54% of the patient had initial Hb 9 – 9.5 gm%

GROUP A FERROUS SULPHATE

Table -2

SMEAR STUDY

S.No.	Smear	No. of Patients	Percentage
1	Microcytic Hypochromic	33	66%
2	Normocytic Hypochromic	9	18%
3	Normocytic Normochromic	8	16%

66% of patient had microcytic hypochromic blood picture

18% of patient had normocytic hypochromic blood picture

16% of patient had normocytic normochromic blood picture

Table -3

GROUP A FERROUS SULPHATE RISE IN Hb

S.No.	Rise in Hb% gm%	No. of patient	Percentage
1	< 1	6	12%
2	1 – 1.5	35	70%
3	1.6 – 2	9	18%

In ferrous sulphate group 70% of the patient showed a increase of 1 – 1.5 gm% 18% of the patients showed a increase of 1.6 – 2gm%. 12% of the patients showed a increase of less than 1 gm%.

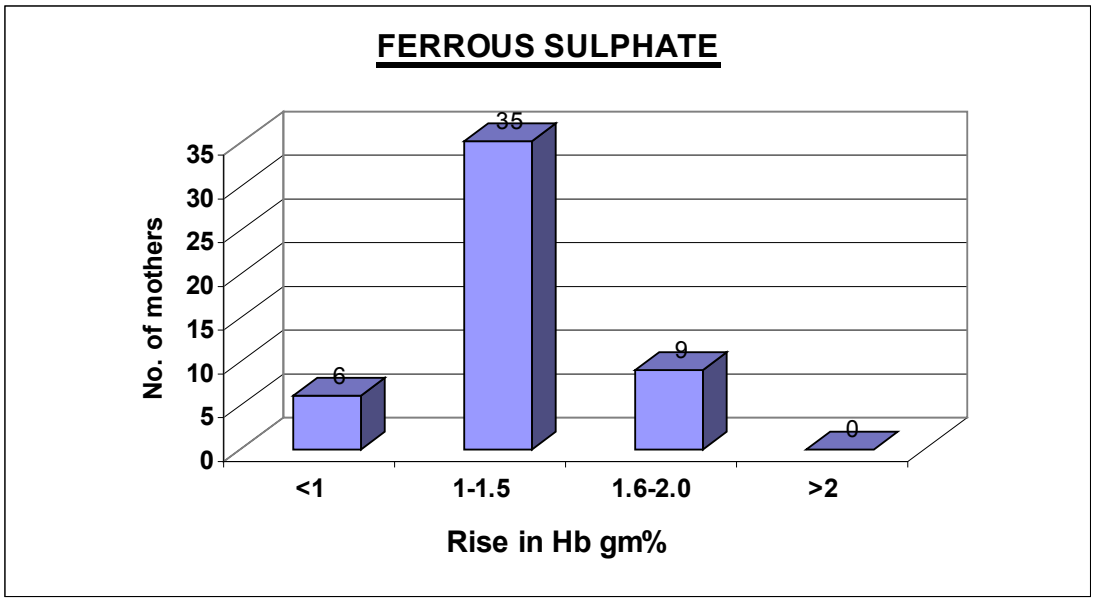

FERROUS SULPHATE
No. of mothers
35
30
25
20
15
10
5
0
6
35
9
0
<1
1-1.5
1.6-2.0
>2
Rise in Hb gm%

Table -4

GROUP A FERROUS SULPHATE SIDE EFFECTS

S.No.	Side effect	No. of patients	Percentage
1.	Epigastric pain	8	16%
2.	Vomiting	2	4%
3.	Constipation	4	8%
4.	Metallic taste	4	8%
5.	Diarrhoea	1	2%
6.	Nil	31	62%

In ferrous sulphate group 62% of patients showed no side effect. 8% of patients had constipation and metallic taste. 2% had diarrhoea.

Table -5

GROUP B SODIUM FEREDETATE

S.No.	Initial Hb% gm%	No. of Patient	Percentage
1	9 – 9.5	25	50%
2	8 – 9	25	50%

In sodium Feredetate 50% of the patients had 9 – 9.5gm% and another 50% of the patients had 8- 9 gm%.

Table -6

GROUP B : SMEAR STUDY SODIUM FEREDETATE

S.No.	Smear	No. of patients	Percentage
1	Microcytic Hypochromic	30	60%
2	Normocytic hypochromic	10	20%
3	Normocytic Normochromic	10	20%

60% of the patient had microcytic hypochromic blood picture.

Table -7

GROUP B : SODIUM FEREDETATE RISE IN Hb

S.No.	Rise in Hb% (gm%)	No. of patient	Percentage of Patient
1	1- 1.5	25	50%
2	1.6 – 2	25	50%

In group B 50% of the patient had a rise of 1 – 1.5gm% and remaining 50% of the patients showed a rise of 1.6 – 2 gm%.

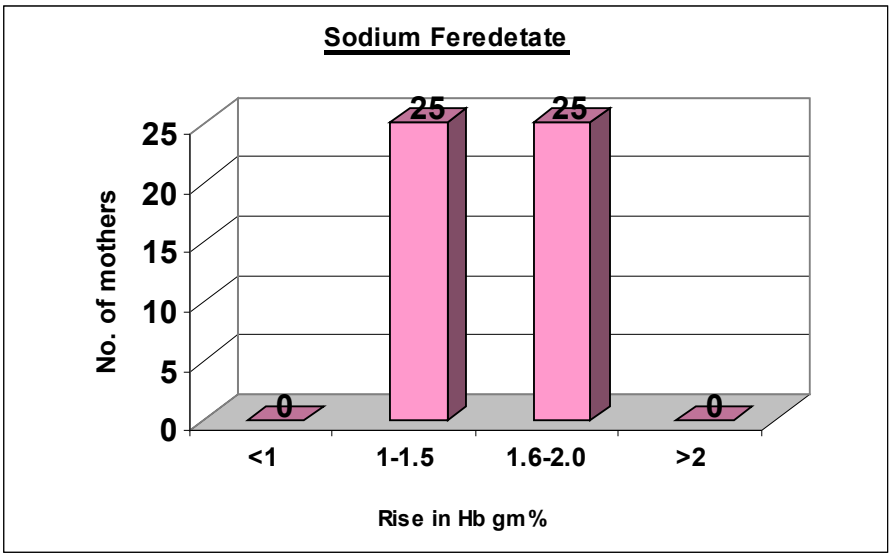

Sodium Feredetate
No. of mothers
25
20
15
10
5
0
25
25
0
0
<1
1-1.5
1.6-2.0
>2
Rise in Hb gm%

Table -8

GROUP B SODIUM FEREDETATE SIDE EFFECTS

S.No.	**Side effects**	**No. of patients**	**Percentage**
1.	Epigastricpain	6	12%
2.	Vomiting	2	4%
3.	Constipation	3	6%
4.	Metallictaste	5	10%
5.	Diarrhoea	-	-
6.	Nil	34	68%

68% of patients in sodium feredetate group showed no side effect. Epigastric pain was present in 12% of patient. Vomiting, constipation and metallic taste contributes to 4%, 6% and 10% of the patients.

Table -9

GROUP C CARBONYL IRON INITIAL Hb%

S.No.	Initial Hb% gm %	No. of patient	Percentage
1	8-9	24	48%
2	9 – 9.5	26	52%

In carbonyl group 48% of patient had initial hamoglobin value 8 – 9gm %, 52% of the patient had initial haemoglobin value 9 – 9.5%.

Table -10

GROUP C CARBONYL IRON SMEAR STUDY

S.No.	Smear study	No. of Patient	Percentage of Patient
1	Microcytic Hypochromic	34	68%
2	Normocytic Hypochromic	13%	26%
3	Normocytic Normochromic	3	6%

68% of the patients had microcytic Hypochrmic blood picture.

Table -11

GROUP C CARBONYL IRON RISE IN Hb%

S.No.	Rise in Hb gm%	No. of patient	Percentage
1	> 2	2	4%
2	1.6 – 2	30	60%
3	1 – 1.5	18	36%

In carbonyl iron group 60% of the patients had a rise in Haemoglobin 1.6 – 2gm%. 4% of the patient had a rise of more than 2gm%, 36% of patients had rise of 1 – 1.5 gm%.

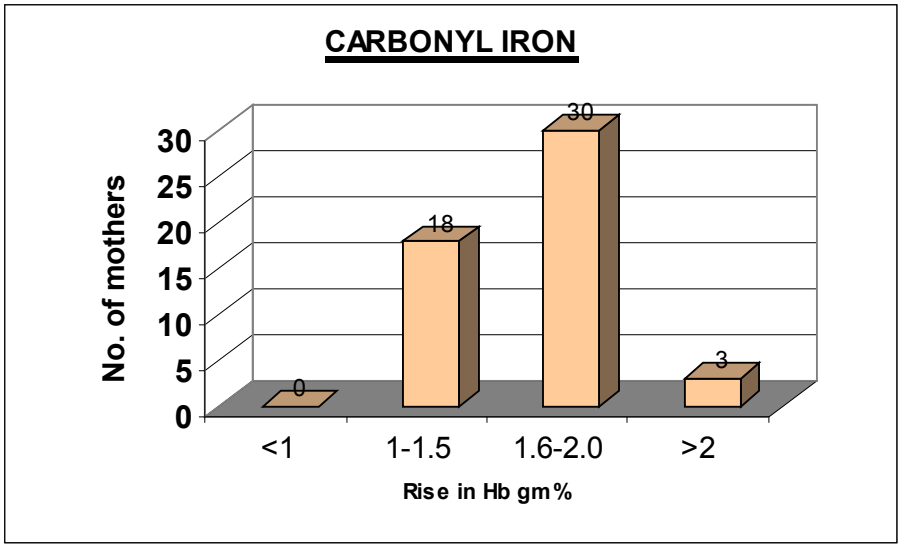

CARBONYL IRON
No. of mothers
30
25
20
15
10
5
0
0
18
30
3
<1
1-1.5
1.6-2.0
>2
Rise in Hb gm%

Table -12

GROUP C : CARBONYL IRON SIDE EFFECTS

S.No.	Side effects	No. of patients	Percentage
7.	Epigastric pain	4	8%
8.	Vomiting	1	2%
9.	Constipation	2	4%
10.	Metallictaste	6	12%
11.	Diarrhoea	1	2%
12.	Nil	36	72%

In carbonyl iron group 72% of the patient had no side effect 2% of the patients had diarrhoea and vomiting. 4% of the patients had constipation. 8% of patient had epigastric pain 12% of the patients had metallic taste.

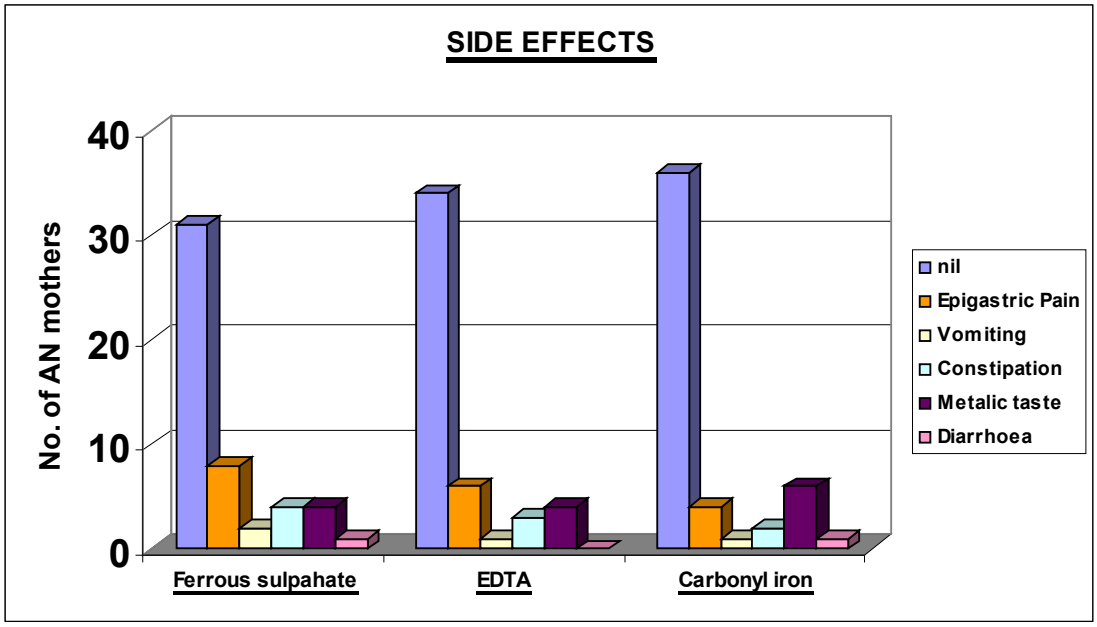

SIDE EFFECTS
No. of AN mothers
40
30
20
10
0
Ferrous sulpahate
EDTA
Carbonyl iron
nil
Epigastric Pain
Vomiting
Constipation
Metalic taste
Diarrhoea

Table -13

GROUP D IMFERON INITIAL Hb

S.No.	Initial Hb% gm%	No. of patient	Percentage
1	8-9	24	48%
2	9 – 9.5	26	52%

52% of patient had initial Hb 9 – 9.5gm%. 48% of patient had initial Hb 8- 9gm%.

Table -14

GROUP D IMFERON SMEAR STUDY

S.No.	Smear study	No. of Patient	Percentage of Patient
1	Microcytic Hypochromic	30	60%
2	Normocytic Hypochromic	18	36%
3	Normocytic Normochromic	2	4%

60% of the patients in group B had microcytic hypochromic blood picture.

Table -15

GROUP D IMFERON RISE IN Hb gm%

S.No.	Rise in Hb gm%	No. of patient	Percentage
1	< 1.5	3	6%
2	1.5 – 1.9	17	34%
3	2 – 2.5	30	60%

In imferon group 60% of the patients had a rise in Haemoglobin 2 – 2.5gm%. 34% of the patient had haemoglobin rise 1.5 – 1.9gm% , 6% of patient showed a rise of < 1.5gm%.

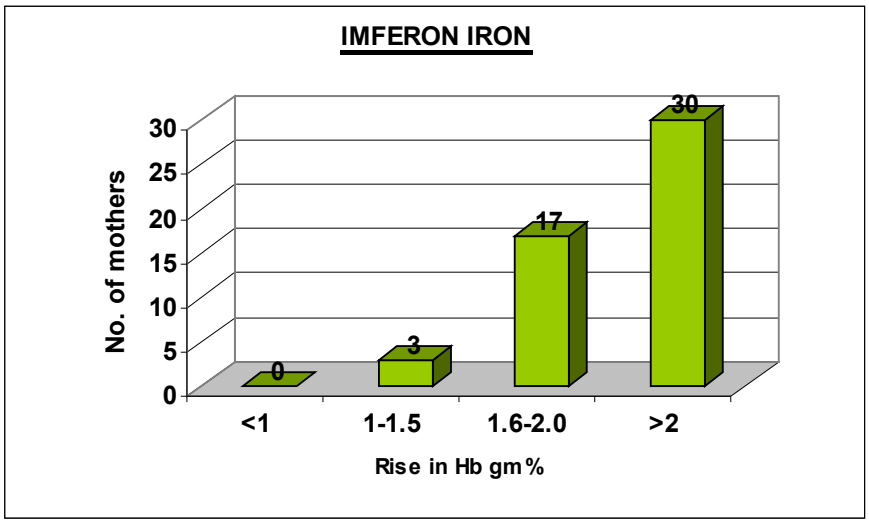

IMFERON IRON
No. of mothers
30
25
20
15
10
5
0
0
3
17
30
<1
1-1.5
1.6-2.0
>2
Rise in Hb gm%

Table -16

GROUP D IMFERON GROUP SIDE EFFECTS

S.No.	Side Effects	No. of Patients	Percentage
1.	Pain at injection site	50	100%
2.	Discolouration of skin at injection site	20	40%
3.	Arthralgia	5	10%

All the patient in imferon group had pain at injection site. 40% of the patients had discolouration of skin at the injection site, 10% of patient had arthralgia.

ANALYSIS AND DISCUSSION

Analysis of data

a) Age

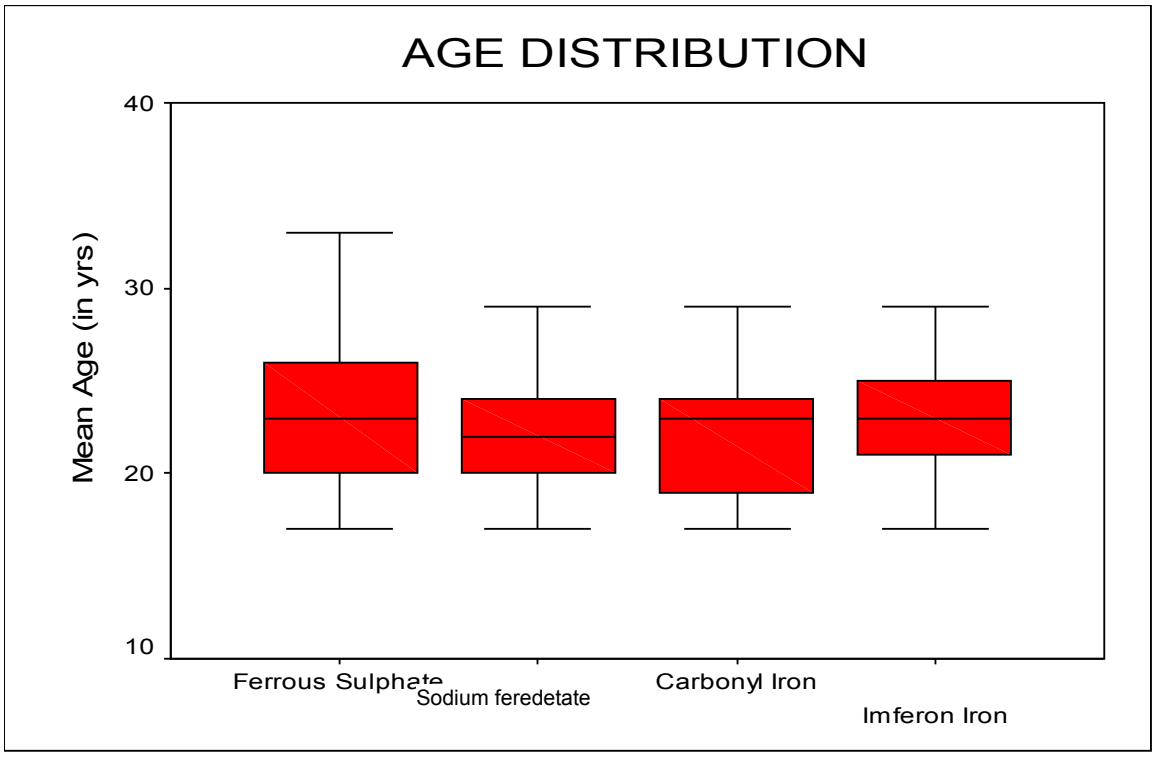
The mean age of patient in each group

Group A Ferrous Sulphate	:	23.86
Group B Sodium Feredetate	:	22.36
Group C Carbonyl Iron	:	22.40
Group D Imferon	:	23.80

Age Distribution

	N	Mean	SD	ANOVA F-test
Ferrous Sulphate	50	23.36	4.144	
Sodium Feredetate	50	22.36	3.397	F=0.87
Carbonyl Iron	50	22.40	4.111	P=0.46
Imferon Iron	50	23.06	3.291	
Total	200	22.80	3.753	

The age was analysed by ‘F test’ the difference was not significant.


AGE DISTRIBUTION
Mean Age (in yrs)
40
30
20
10
Ferrous Sulphate
Sodium feredetate
Carbonyl Iron
Imferon Iron

Analysis of Body Mass index :

The Mean Body Mass index in each group

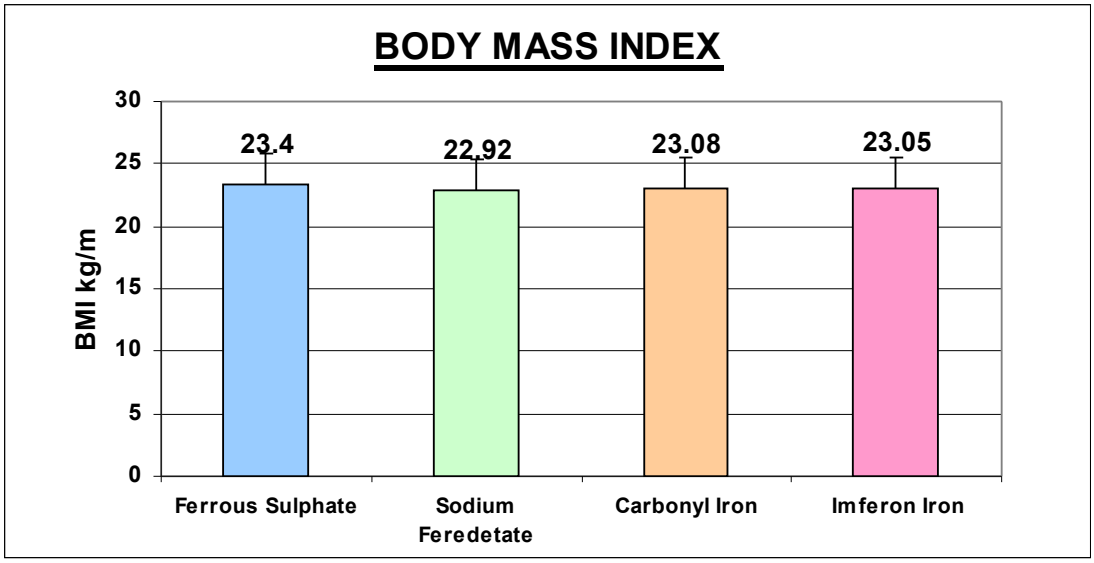
Group A Ferrous Sulphate	:	23.40 kg/m^2
Group B Sodium Feredetate	:	22.92 kg/m^2
Group C Carbonyl Iron	:	23.08 kg/m^2
Group D Imferon	:	23.05 kg/m^2

BMI

	N	Mean	Std. Deviation	ANOVA F-test
Ferrous Sulphate	50	23.40	3.220	
Sodium Feredetate	50	22.92	2.578	F=0.46 P=0.87
Carbonyl Iron	50	23.08	3.185	
Imferon Iron	50	23.05	2.734	
Total	200	23.11	2.926	

This was also analysed with ‘F Test’, F – 0.46, P – 0.87.

The difference was not significant.


BODY MASS INDEX
BMI kg/m
30
25
20
15
10
5
0
23.4
22.92
23.08
23.05
Ferrous Sulphate
Sodium Feredetate
Carbonyl Iron
Imferon Iron

Analysis of Gestation age :

The mean gestational age in each group

Group A Ferrous Sulphate	:	27.40 weeks
Group B Sodium Feredetate	:	27.44 weeks
Group C Carbonyl Iron	:	27.48 weeks
Group D Imferon	:	27.54 weeks

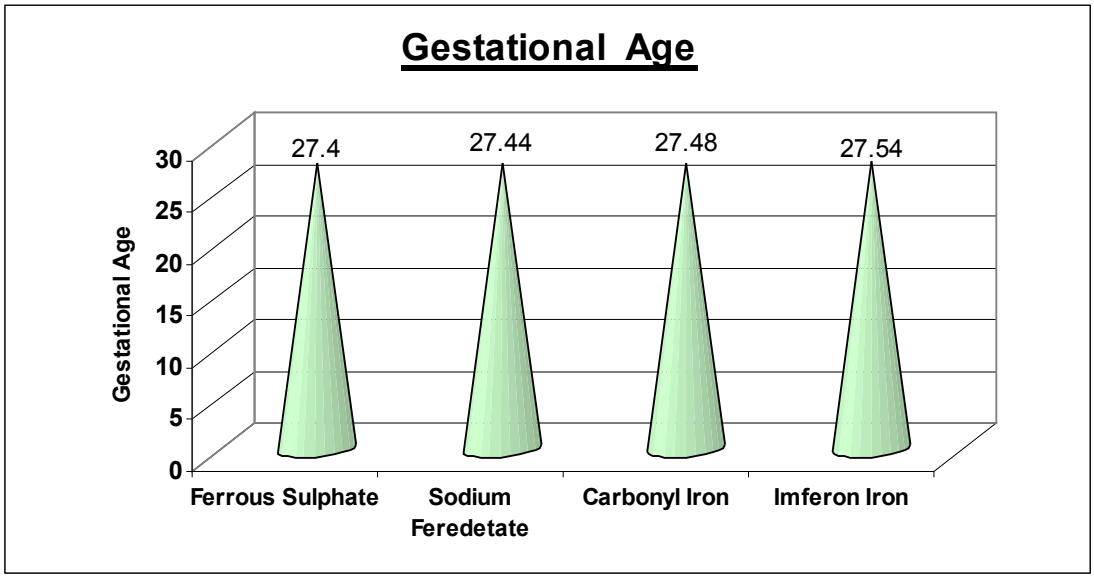
Gestation Age

	N	Mean	Std. Deviation	ANOVA F-test
Ferrous Sulphate	50	27.40	2.921	
Sodium Feredetate	50	27.44	2.998	F=0.46
Carbonyl Iron	50	27.48	2.880	P=0.87
Imferon Iron	50	27.54	2.991	
Total	200	27.47	2.926	

The difference was not significant

F = 0.46

P = 0.87


Gestational Age
Gestational Age
30
25
20
15
10
5
0
27.4
27.44
27.48
27.54
Ferrous Sulphate
Sodium Feredetate
Carbonyl Iron
Imferon Iron

Analysis of Initial Haemoglobin

Mean Initial Haemoglobin in Each Group

Group A Ferrous Sulphate	:	8.854 gm%
Group B Sodium Feredetate	:	8.770 gm%
Group C Carbonyl Iron	:	8.808 gm%
Group D Imferon	:	8.712 gm%

Initial HB

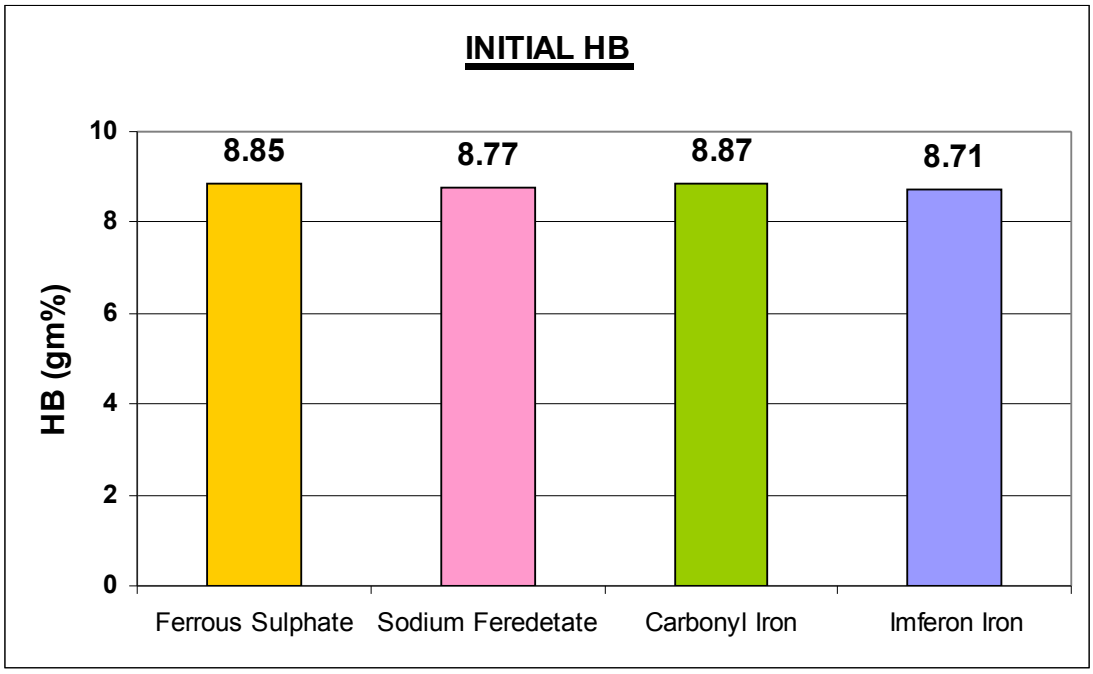
	N	Mean	Std. Deviation	F-test
Ferrous Sulphate	50	8.854	.4509	
Sodium Feredetate	50	8.770	.4362	F=0.95 P=0.42
Carbonyl Iron	50	8.808	.4285	
Imferon Iron	50	8.712	.4260	
Total	200	8.786	.4354	

One way Analysis of Variance F-test

The difference was not significant proved by F test

F = 0.95

P = 0.42


INITIAL HB
HB (gm%)
10
8
6
4
2
0
8.85
8.77
8.87
8.71
Ferrous Sulphate
Sodium Feredetate
Carbonyl Iron
Imferon Iron

COMPARISON OF INCREASE IN HAEMOGLOBIN

The gestational age, initial haemoglobin, Bodymass index, being equalized in each group increase in Haemoglobin in each group was analysed.

Group A Ferrous Sulphate group :

70% of the patient showed 1 – 1.5gm% increase

Group B sodium Feredetate group :

50% of the patient showed 1 – 1.5 gm% increase

50% of the patient showed 1.6 – 1.9 gm% increase

Group C Carbonyl Iron

60% of the patient showed 1.6 – 2gm% increase

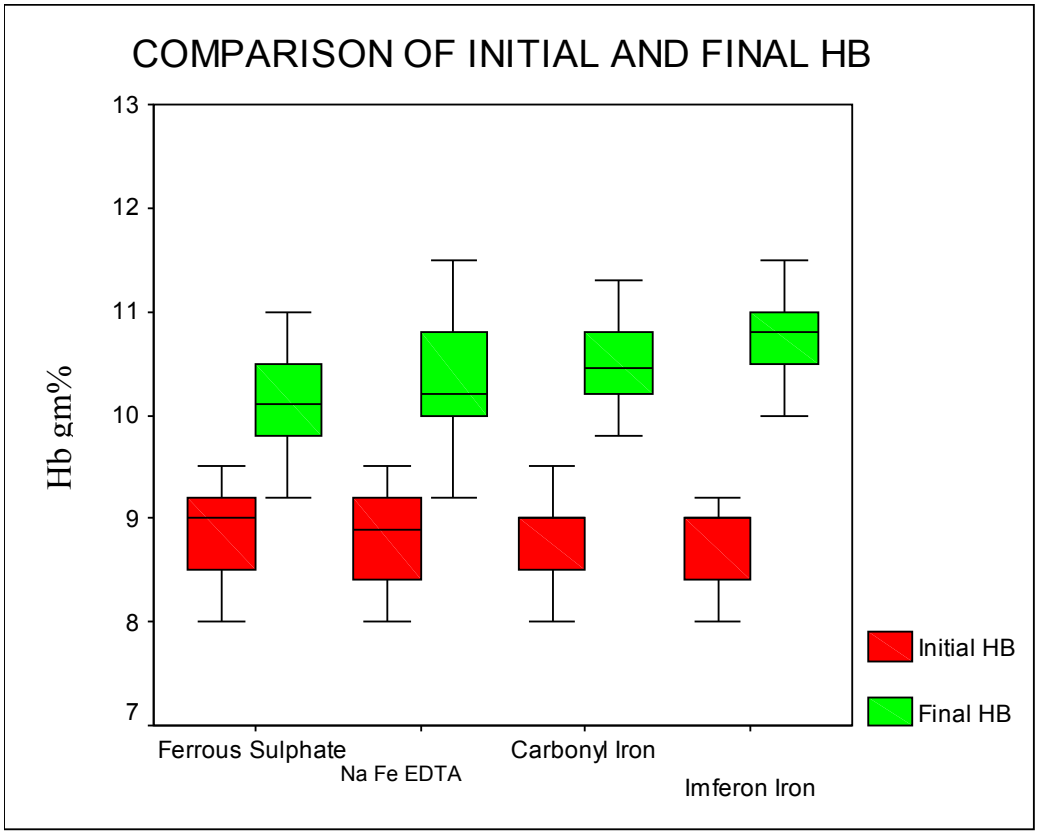
Group D : Imferon group

60% of the patient showed 2 – 2.5gm% rise

Increase in Hb

Group	INCREASE				Total
	<1.0	1.0-1.5	1.5-2.0	>2.0	
Ferrous Sulphate	6	35	9	0	50
Sodium Feredetate	0	25	25	0	50
Carbonyl Iron	2	15	30	3	50
Imferon Iron	0	3	17	30	50

$\chi 2=96.6$ P = 0.001 P value is significant


COMPARISON OF INITIAL AND FINAL HB
Hb gm%
13
12
11
10
9
8
7
Ferrous Sulphate
Na Fe EDTA
Carbonyl Iron
Imferon Iron
Initial HB
Final HB

Comparison of Increase in Hb%

S.No.	Group	Initial	Final	Difference	Paired t - test
1.	Ferrous sulphate	8.85 ± 0.45	10.07±0.44	1.214±0.35	T=24.6 P=0.001
2.	Sodium Feredetate	8.77±0.44	10.25±0.48	1.484±0.31	T=34.2 P=0.001
3.	Carbonyl iron	8.81 ± 0.42	10.47 ± 0.37	1.660 ±0.32	T = 37.8 P = 0.001
4.	Imferon iron	8.71 ± 0.43	10.75 ± 0.45	2.038 ± 0.33	T = 43.7 P 0.001

The imferon group showed a better rise in haemoglobin than oral group. Carbonyl iron showed a better response than sodium Feredetate and ferrous sulphate group. The increase in haemoglobin was analysed using paired 'T' test. The above statement was proved. P values is significant.

DISCUSSION

Anaemia is the commonest medical disorder in pregnancy. Iron deficiency can be corrected by administration of iron. The goal of treatment is to increase haemoglobin levels as rapidly as possible.

Ferrous sulphate is the prevalent iron available in all Government Institution and so the result obtained with other three iron is compared with ferrous sulphate.

In our study only moderately anaemic patient are selected due to ethical reasons that severely anaemic pregnant women needs blood transfusion and repeated intramuscular injection. In our study all cases came for follow up.

Smear study in all the four groups of iron showed maximum of microcytic hypochromic type blood picture, next to that is normocytic hypochromic blood picture, is found in majority of patient which showed that nutritional iron deficiency anaemia is common in our antenatal mothers.

In our study parentral group i.e. imferon group showed a better rise in haemoglobin than oral group, 60% of the patient in imferon showed a rise of 2 – 2.5gm where as 70% of the patient in ferrous sulphate group showed a rise of 1 – 1.5gm%.

In a WHO sponsored collaborative studies on Nutritional anaemia in India by Sood SK, Ramachandran K, Rani – K, Ramalingasamy, greater increase in haemoglobin was obtained with parentral administration of iron than with oral group.

In ICMR study conducted at Department of Obstetric and Gynaecology KGMU, Lucknow by Srivastava Aarti, Tandon prabba short intermuscular iron therapy improves haemoglobin levels, built up iron stores and maintains the rise till delivery better than oral iron.

Among the oral group carbonyl iron showed a better response than ferrous sulphate and sodium Feredetate.

60% in carbonyl iron group showed a rise of 1.6 – 2gm% where as in ferrous sulphate 70% showed a rise of 1 – 1.5gm%.

A randomized double blind study regarding bioavailability of carbonyliron was done in female blood donors with iron deficiency anaemia overall bioavailability of carbonyl iron is 70% that of ferrous sulphate. The study was conducted in Department Of Medicine Ohio Western Research University. By Devasthali SD, Godeuk VR, Brittenhan GM.

Process of carbonyl iron absorbtion in rat duodenal mucous studied with imunostaining for ferritin done in Department of Pathology Okayama University, Japan. Showed that liver ferritin is increased after oral administration of Carbonyl iron. Proving a better bioavailability.

High dose carbonyl iron for iron deficiency anaemia a randomized double blind trail conducted by Gorduk V.R., Brittenham showed safety of carbonyl iron with large doses. The study concluded carbonyl iron is an effective inexpensive treatment for iron deficiency anaemia is accompanied by

tolerable side effects and may have advantage over other iron salts by decreasing risk of iron poisoning in children.

In our study sodium Feredetate showed a better response than ferrous sulphate 50% of the patient in sodium Feredetate group showed 1.6 – 2gm% rise where 60% of the patient in ferrous group showed a risk of 1 – 1.6gm%. This was due to better absorbtion of iron mediated by chelator EDTA.

Our results was substantiated by following other studies.

The effect of different iron fortificant in iron fortified rice. Iron absorbtion from rice fortified with different iron fortificants. Eg., ferrous sulphate, sodium feredetate, ferrous fumarate with radio labeled istope was studied by Trinidad TP, Valdez DH, Iron absorbtion was better with rice fortified with sodium feredetate

Potential role of sodium feredetate as iron fortificant was done in Department of Medicine Faculty of Health Science, University of Witwatersrand in South Africa. Showed sodium EDTA in the dose range of food fortificant does not have toxic effect. FAO/WHO expert committee on food additives concluded that Na EDTA was safe in fortification programme.

In our study regarding the side effect gastrointestinal side effects were more common in the oral group than the parentral group. In the parentral group all the patients complained of pain at injection site, discoloration of skin at injection side and arthralgia. None had severe reaction like allergy, itching,

fever or anaphylaxis. In Imferon group to all those patient who complained on pain and arthralgia small doses of analgesic were prescribed.

Among the oral group. Gastrointestinal side effect was predominantly complained.

38% of patient in ferrous sulphate group

32% of the patient in sodium feredetate

28% of the patient in carbonyl iron group.

The study drugs were well tolerated in all the group. All those patient who complained epigastric pain were asked to take the tablet along with food, constipation was managed by asking the patient to take high fibre diet. Vomiting and diarrhoea subsided within 3 to 4 days by itself no specific medication was given to the patient to stop that reaccurance and education about anaemia was given to all those patient who complained of side effect.

Cost Benefit Analysis:

The cost of Imferon amounts to Rs.100/- the syringes and needles account for about Rs.90/-. The diclofenac tablet prescribed for side effect amount to Rs.5 to Rs.10 total cost of treatment in parental group cost around Rs.200/- for 1 month/ patient.

The cost of ferrous sulphate tablet account to Rs.75/- for 1 month / patient. The cost of carbonyl iron for 1 month amounts to Rs.300/- the cost of sodium Feredetate for 1 month / patient amounts to Rs.240/- for month / patient,

Among oral iron carbonyl iron was expensive than other two group. But our study we found 70% of the patient in ferrous sulphate showed rise of 1 – 1.5gm% which is not bad. In a country like ours where anaemia is widely prevalent anaemia can be cured with ferrous sulphate which is available free of cost in all Government set up and Primary Health Centres.

In our study advantages noted with oral iron group are

a) Needs no hospitalization for test dose

b) Needs no assistance of paramedical workers

c) Lower expenditure than parentral (ferrous sulphate)

d) Carbonyl iron shows better response with rise of 1.54 – 2gm%.

Disadvantages of oral group in our study :

a) Gastrointestinal side effects is noted

b) Patient needs reassurance and treatment of side effects during their visit at 2 weeks of treatment.

c) Prolonged treatment is needed

d) Haemoglobin rise was more in parentral group.

e) Carbonyl iron treatment is more expenditure than parentral iron

Advantages of Parental Iron :

1. Iron administered as injection bypasses the Gastrointestinal tract so the compliance is good due to lack of gastrointestinal side effects.

2. Better rise of haemoglobin percentage
3. Treatment period is short.

In our study disadvantage of Parentral Group

1. Need for assistance in administrating the drug
2. Cost factor
3. Pain and Discolouration at injection site.

SUMMARY

Ferrous Sulphate	-	70% of the patient had 1 – 1.5 gm% rise in haemoglobin per month
Sodium Feredetate	-	50% of the patient had 1.6 – 2 gm% rise in haemoglobin per month
Carbonyl iron	-	60% of the patient had 1.6 – 2 gm% rise in haemoglobin per month
Parentral iron	-	60% of the patient had a rise of 2 – 2.5gm% per month

- Parentral group showed a better response than oral group.
- Among oral iron, carbonyl iron showed a better response.
- Expenditure of treatment was more with carbonyl iron.
- Ferrous sulphate was the cheaper iron.
- Gastro intestinal side effects was noted in all three groups of oral iron
- Pain and discoloration of skin was complained by the parentral group.
- Parentral iron administration needs hospitalization and the help of paramedical workers

CONCLUSION

In our study among the oral groups efficacy of carbonyl iron and sodium feredetate is more than ferrous sulphate but the expenditure of treatment is higher than ferrous sulphate which the patients in our setup cannot afford. The ferrous sulphate group showed a 1 – 1.5gm% rise in haemoglobin / month, when screened at a earlier gestational age (24 – 32 weeks) anaemia of moderate grade can be effectively treated with ferrous sulphate at a lower cost.

The compliance and efficacy of parentral iron dextran is more than all three oral groups. If the patient cannot tolerate oral iron we can change over to parentral iron which showed a better rise in haemoglobin.

PROFORMA

Patients Name :

Address :

Age :

Obstetric Status :

LMP :

EDD :

Ht Wt BMI

Gestational Age :

Type of Iron :

Date of Starting Therapy :

Past History :

History of any disease in the past Yes No

If yes Specify the disease

Clinical Examination

USG

Investigation :

1. Peripheral Smear
2. Haemoglobin % Day 0 Day 30

Side effects noted :

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