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# Iron Sucrose Fixed Dose - A 'Sprint' Therapy For The Treatment Of Iron Deficiency Anemia In Obstetric And Gynaec Patients

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**ABSTRACT**

*Objectives: To study the efficacy and safety of fixed dose intravenous iron sucrose therapy in the treatment of iron deficiency anaemia in obstetric and gynaecological Patients. Method: Well compensated anemic patients with Hb between 5 9 gm% were included in the study. Patients were thoroughly investigated for hematological parameters. Each patient has received a fixed dose of 600 mg iron sucrose IV divided in three such doses every alternate day, followed by oral iron therapy to replenish the iron stores. Results: Average rise in Hb in moderate anemia group is 1.85, 2.60 & 3.40 gm% after 7, 14 & 28 days respectively after infusion. In severe anemia group Hb rise observed is 2.50, 3.73 & 4.70 gm% after 7, 14& 28 days respectively. Significant improvement in iron stores is also observed at the end of 28 days. Paired 't' test and 'Z' test was used to test the significance of rise . Conclusion: Fixed dose iron sucrose and subsequent oral iron therapy is very useful for raising Hb rapidly and safely in patients with moderate and sever iron deficiency anemia.*

**Key word : Iron Sucrose, Fixed Dose, Iron Deficiency Anemia.**

## Introduction

Iron deficiency anemia is the commonest medical disorder seen in obstetric and gynecological patients; with prevalence of around 70% in pregnant and 30-50% in non pregnant females in developing countries like ours. Anemia is estimated to contribute 20 percent of all maternal deaths and nine times higher risk of perinatal mortality. The odds for low birth weight are tripled, while those for preterm delivery more than doubled in association with IDA. Anaemia and iron deficiency in pregnancy are associated with large placental weight and a high ratio of placental weight to birth weight (placental ratio), both of which are predictors of adult hypertension.

As compliance to oral iron therapy is very poor and also the results are unpredictable, injectable iron therapy is better option to treat such patients. Various compounds like iron dextran (IM/IV) , iron sorbitol (IM), iron sucrose(IV), etc are available for injectable therapy of which iron sucrose gives better results because of less chances of hypersensitivity reactions(no test dose required), quick binding of iron to transferrin and quick travel to bone marrow resulting in early rise in Hb. So we have prospectively monitored the response to fixed dose IV iron sucrose in a cohort of 107 highly motivated pregnant women and gynaec patients over a four week period.

## Material & Methods

It is a prospective, randomized, study without blinding. The study was conducted in Dept. of OBGY Smt Kashibai Navale Medical College & General Hospital, Pune from Jan 2010 to Dec 2010 after ethical committee approval. All the well compensated patients with moderate to severe anemia (Hb 5-9 gm %) were included in this study; the patients were selected from those attending obst. and gynaec. OPD.

Inclusion Criteria:

- Patients with Hb between 5-9 gm%
- Patients with iron deficiency anemia only (peripheral smear showing microcytic hypochromic picture, low sr. iron, & ↑ TIBC)

Exclusion Criteria:

- Any hematological disorder other than Iron Deficiency Anemia
- Patients suffering from chronic illness like renal, cardiac, hepatic or immunological disorders
- Known hypersensitivity and resistance to injectable iron compounds
- Patients with severe anemia in decompensated state requiring blood transfusion.
- Pregnant patients with gestational age < 12 weeks and > 36 weeks.

Written & informed consent was taken after counseling. All the consequences & benefits of the therapy are explained to patient. After inclusion in study detailed history of each patient was taken including age, medical history, obstetric history, menstrual history & family history. Detailed physical examination was carried out; along with investigations like hemogram, reticulocyte count, Hct, MCV, MCHC, MCH, RDW, peripheral smear, Sr. iron and TIBC.All the hematological parameters were done on peripheral venous blood (collected from cubital vein) by colorimetric method using automated Beckman Coulter apparatus and Sr. Iron, TIBC was done by Coral kit (ferrozine method).

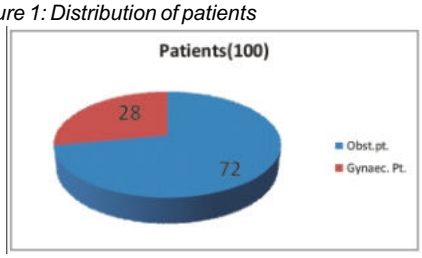
Prior to commencing iron therapy, all women were de-wormed with two tablets of Mebex Plus, a combination of Pyrantyl Palomate and Mebendazole (Cipla India Pvt Ltd).

Iron sucrose (Emcure Pharmaceuticals Ltd. Pune India) 200 mg diluted in 100 ml of NS given slow IV over 1 hr and three such doses every alternate day was given to every patient on indoor basis. Iron sucrose of same brand was used for each patient. During and 1 hour after infusion each patient was monitored on 1:1 basis in the ward for any adverse reactions. All the oral iron preparations are suspended at least 24 hours prior to infusion to avoid reactions and again restarted 48 hrs after completion of therapy. After completion of the regimen patients were discharged from ward and followed up on the OPD basis weekly for 4 weeks from the day of completion of therapy. After this fixed dose regimen we have prescribed 100 mg of ferrous ascorbate and 1.5 mg of folic acid (Tab.Orofer XT, Emcure Pharmaceuticals Ltd. Pune India) per day orally to all our patients during follow up, to replenish the iron stores. We encouraged, but did not seek to monitor compliance because that is not done in routine clinical practice. Each patient was followed for Hb rise by weekly testing for Hb and all the parameters on admission are repeated 28 day after completion of therapy; the results were noted in preformed Performa for each patient and tested stastically at the end of study by using paired 't' test and 'Z' test. Any adverse drug reactions during infusion and in follow up period were recorded.

**Results**

Actual patient recruitment started in 1st week of feb.2010 after ethical committee approval. 107 patients registered; of which 100 have completed follow up. 7 patients were lost to follow up for variety of reasons (one aborted at three weeks after recruitment; and 6 did not turn up for their follow up Hb estimation at 4 weeks either because they had moved out of the city or they presented later than four weeks ). Results are encouraging with early rise in Hb, good patient satisfaction, minimal side effects and easy administration of dose. Out of 100 patients 72 were obstetric 28 were gynaec patients.

*Figure 1: Distribution of patients*




Patients studied were from all the age groups and most patients were belonged to age group of 20-25 years. DUB followed by Fibroids was the most common diagnosis in gynaec patients [Table 1]. Most of the obstetric patients were primigravida and in the 2nd trimester of pregnancy [Table 2].

*Table 1: Diagnosis in gynaec patients*

| | Total (n) = 28 | |
|---|---|---|
| Diagnosis | n | % |
| DUB | 12 | 42 |
| Prolapse | 03 | 11 |
| Postmenopausal bleeding | 02 | 07 |
| Leiomyoma | 07 | 25 |
| Adenomyosis | 04 | 15 |

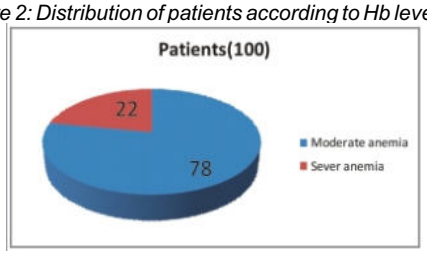
*Table 2: Distribution of obstetric patients according to gestational age*

*Most of the patients were in 2nd trimester of pregnancy. The drug was not used in patients with less than 12 weeks gestation (safety not proved) and >36 weeks gestation.*

*Response to fixed dose iron sucrose in moderate anaemia group*

Out of 100 patients completed follow up in our study; most of the patients (78%) were in moderate anemia (Hb 7-9 gm %) group as they were hemodynamically stable and can be easily treated by injectable iron therapy. Most of the patients were obst. patients in moderate anemia group

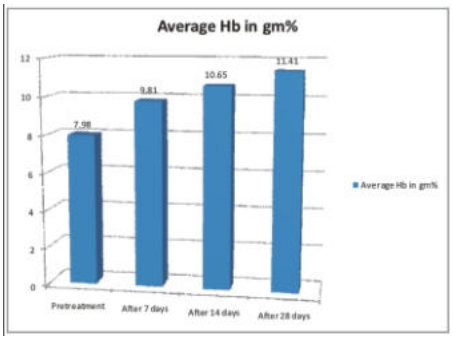
*Figure 2: Distribution of patients according to Hb levels*




a) Rise in Haemoglobin level

Haemoglobin rise in these patients after fixed dose therapy is significant after 7 days average rise is 1.9 gm% (range 0.8 3.9, SE= 0.141 in 95% CI, Z= 12.77, P<0.01); after 14 days average rise is 2.7 gm% (range 1-4.6, SE=0.1844 in 95% CI, Z=14.48,P<0.01); after 28 days average rise is 3.42 gm% (range 1.3-6.3, SE= 0.152 in 95% CI, Z=22.5,P<0.01)

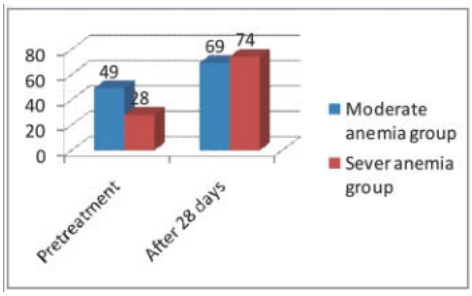
*Figure 3 : Hb rise after fixed dose iron sucrose therapy in moderate anemia group*




b) Improvement in iron stores

Statically significant improvement in iron stores with average serum iron level of 49 microgram/dl at the time of recruitment increased up to 69 microgram/dl after 28 days. Serum TIBC levels were decreased from average 489 microgram/dl to 315 microgram/dl after 28 days of therapy.

*Figure 5: Improvement in iron stores - moderate anemia group*



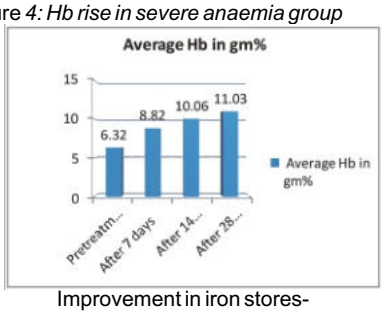

*Response to fixed dose iron sucrose in severe anaemia group*

22 patients from severe anaemia group (5- 7 gm %) were hemodynamically stable and completed follow up.

a) Rise in haemoglobin level

Haemoglobin rise is statically significant after fixed dose iron sucrose therapy after 7 days average rise is 2.71 gm% (range 1.6-3.7, SD 0.67, t= 17.40 at 21 DF); after 14 days average rise is 4 gm% (range 2.8-7.2,SD 1.11,t=15.79 at 21 DF) and after 28 days average rise is 4.9 gm%( range 3.5-7.5,SD 1.075,t=20.55 at 21 DF).

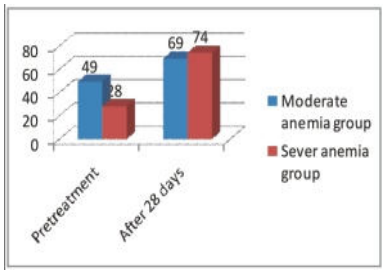
Figure *4: Hb rise in severe anaemia group*




b) Improvement in iron stores-

Improvement in iron stores is statically significant with serum iron level increasing from average 28 microgm/dl at the time of recruitment to 74 microgram/dl after 28 days and fall in total iron binding capacity from average 530 microgm/dl at recruitment to 376 microgm/dl after 28 days.

*Figure 5: Improvement in iron stores - moderate anemia group*




*Adverse reactions to iv iron sucrose:*

Minor adverse reactions, which included burning at the infusion site , itching ,giddiness and GI symptoms like nausea and vomiting, occurred in 15% of the women, but there were no major adverse reactions .

*Table 3: Adverse Drug Reactions Observed*

| | |
|---|---|
| Rigors | 1 |
| Fever | 0 |
| Headache, light headedness | 1 |
| Flushing or any other skin eruption | 0 |
| Itching | 3 |
| Hyper/hypotension, | 0 |
| Chest pain , breathlessness | 0 |
| Injection site problem. E.g. pain, redness ect. | 8 |
| Nausea, vomiting, diarrhea | 2 |
| Sever life threatening anaphylactic reaction | 0 |

## Discussion

World Health Organization recommends Hb concentration value of minimum 11 gm% during pregnancy. According to this definition incidence of anemia is very high in developing tropical countries like ours where it remains a major contributing factor to maternal morbidity and mortality and also high perinatal mortality. The major concern about the adverse effects of anemia on pregnant women is the belief that this population is at greater risk of perinatal mortality. An association between maternal anemia and low birth weight infants as well as preterm delivery has been found in various studies. The often unrecognized consequence of maternal IDA is the impact on the foetus, newborn, child and subsequent adult.

In our gynecological patients who are for major surgeries anemia is very common, by giving IV iron sucrose therapy it is possible to effectively raise Hb in very short span of time thus reducing or completely eliminating need for perioperative blood transfusion with its inherent complications. Adequate pre and post operative Hb conc. will improve the patients prognosis after any surgery.

In the developed world it has long been documented that intravenous iron supplementation is highly effective in treating IDA in a variety of settings, including pregnancy. There is irrefutable evidence that compared to oral iron, iv iron sucrose results in a much more rapid resolution of IDA, has minimal side-effects, and because it is administered intravenously, it circumvents the problems of compliance. So we have tried to treat IDA with initial 'Sprint' of fixed dose iron sucrose followed by oral ascorbate therapy. As even after calculating TDI by standard formula; most of our patients will require a dose of around 600- 800 mg due to low body weight and surface area, so we have used a fixed dose instead of calculating TDI for each patient; for the ease of administration and logistic purpose. We deliberately did not seek to calculate the optimal iron sucrose dose for each woman based on her Hb level: we simply sought to assess response to a uniform dose in all women whose Hb fell between 5-9g/dl, with an eye to the long term possible adoption of a single universal dose that might go a long way treating IDA in various patients.

## Conclusion

Fixed dose iron sucrose therapy is very useful for raising Hb rapidly and safely in patients with moderate and sever iron deficiency anemia. Using fixed dose avoids cumbersome TDI calculation and prevent wastage of resources(drug). Subsequent treatment with oral iron therapy after fixed dose IV iron sucrose is necessary to replenish the iron stores. Intravenous iron sucrose may be the solution for treating IDA rapidly and safely, large scale trials will be required to establish its full place and potential.

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