To study the efficacy safety and compliance of iron sucrose in mild, moderate and severe anemia in antenatal patients

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Abstract

Introduction: Anaemia is a major public health problems in developing world. Anaemia is a pathological condition in which the oxygen binding capacity of red cells is insufficient to meet the body's need. Anaemia is the most common medical disorder complicating pregnancy. It may antedate pregnancy, often aggravated by pregnancy and delivery. More than 70% of pregnant women suffer from nutritional anaemia in South East Asia. Of all the anaemias diagnosed during pregnancy 75% are due to iron deficiency. The prevalence of anaemia is 55% among expectant mothers across the world and the incidence in India varies from 40 –90% according to WHO reports.

Materials and Method: The prospective study was carried out in the department of obstetrics and Gynecology, in Konaseema institute of medical science Amalapuram during 2015 -16 to access the efficacy, safety and compliance of injectable iron sucrose in pregnancy with mild, moderate and severe iron deficiency anaemia for a period of 12 months from Nov 2015 to Nov 2016.

Result: Among the total number of 104 patients studied, mean age of the study group was 25.4 ± 3.26 years. Teen age pregnancies with anaemia formed 5.7% of the study group. Most cases, i.e. 77.9% were between 20 – 30 years. Elderly gravidas comprised 16.4%. The mean Hb% on day of Admission was 7.670 gm% which raised to 10.388 on day 28 of completion of iron therapy. Thus the mean Hb rise on day 28 was 2.718 gm% which is statistically significant (p value being 0.000).The Hb level at 38 weeks of gestation is 9.162 which is significantly higher when compared with Hb value on the day of admission (p value being 0.000).

Discussion: Haemoglobin values varied significantly with time between groups (interaction effect, p<.001). The change in haemoglobin from baseline was significantly higher on the 14th (p=.004) and 28th (p=.031) days. Ferritin values were higher in the patients receiving intravenous iron throughout pregnancy. No serious adverse drug reactions were observed. Fetal weight and hospitalization time were similar in the 2 groups. Blood transfusion was required for only one patient in the oral group. Thus, it is observed that iron deficiency anemia of pregnancy treated with the intravenous iron had restored iron stores faster and more effectively than oral iron with no serious adverse reactions.

Keywords: Anaemia, Iron sucrose, Antenatal

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Introduction

Anaemia is a major public health problems in developing world. Anaemia is a pathological condition in which the oxygen binding capacity of red cells is insufficient of meet the body's need.(1) Anaemia is the most common medical disorder complicating pregnancy. It may antedate pregnancy, often aggravated by pregnancy and delivery. More than 70% of pregnant women suffer from nutritional anaemia in South East Asia.(2) Of all the anaemias diagnosed during pregnancy 75% are due to iron deficiency.(3) The prevalence of anaemia is 55% among expectant mothers across the world and the incidence in India varies from 40 –90% according to WHO reports.(1) According to WHO, anaemia contributes 40% of maternal deaths in third world countries and in India, it contributes for 10-15% of direct maternal deaths.(4) Iron deficiency anaemia is caused primarily by inadequate intake, faulty dietic habits, inadequate absorption, multiparity. Previous menorrhagia, worm infestation, chronic diarrhoea, chronic malaria, asymptomatic bacteriuria. The demand of iron increases markedly specially after the 2nd trimester, which cannot be met by dietary source alone. The adult human body contains about 3-4 gm of Iron, or which about 60-70% is present in blood (Hb Iron) as circulating iron and rest as storage iron.(5)

The total daily loss of iron of an adult is about 1 mg, and about 12.5 mg per 28 days in menstruating women.

Iron requirement increases during pregnancy from 21 mg / day of standard Indian women to 35 mg/day in pregnant women.(4)

Iron requirements during Pregnancy

The iron requirement of pregnancy for a non-anaemic woman with Hb of 11 mg /dl and body weight of 50 kg can be calculated as follows:

Basal losses of iron from the body	@ 0.8 mg /day	230 mg
Fetus and placenta		360 mg
Expansion of blood volume (by approximately 35%)	@ 1.2 (expansion from 3.5 L to 4.7L) x 110 (Hb in gm /L) x 3.4 (mg Fe /g of Hb)	448 mg
	Total	**1038 mg**
This is besides the iron loss that occurs due to blood loss during parturition.		

(Ref. AJCN. 2004, 79,1-3)

Iron absorption from a habitual Indian diet is less than 5%.[4] Although the iron absorption increases during pregnancy, still it is not sufficient to meet the requirement. So one of the primary aim of antenatal care is to prevent and treat anaemia during pregnancy. As per the recommendations National Nutritional Anaemia Control Pretnancy (NNACP, 1970), every pregnant women should receive 1 adult dose tablet per day for 100 days during her pregnancy. Each tablet contains 100 mg of elemental iron and 500 mg of Folic Acid after the first trimester of pregnancy. Among the pregnant women, non-adherence to oral iron therapy is as high as 32% after 2 months of administration.[6] Oral iron has the disadvantages like poor absorption, poor compliance and gastrointestinal side effects. IV iron is a treatment option for treating mild, moderate and severe iron deficiency anaemia during pregnancy. It also help to restore the iron stores faster and more effectively than oral iron. Previously IV preparation like iron dextran was used with frequent adverse drug reactions.

Now better drugs like Iron-Sucrose is available. Iron sucrose is a safer alternative to iron dextran. The incidence of anaphylaxis and other adverse reaction are much less with excellent safety profile. Correction of iron deficiency is incomplete without replacement of iron stores. So additional 500mg iron should be infused to replenish iron stores.

Materials and Method

The prospective study was carried out in the department of obstetrics and Gynecology, in Konaseema institute of medical science Amalapuram during 2015 -16 to access the efficacy, safety and compliance of injectable iron sucrose in pregnancy with mild, moderate and severe iron deficiency anaemia for a period of 12 months from Nov 2015 to Nov 2016.

Inclusion Criteria:

- Pregnant women between 16 wks to 32 wks with
- Mild (8 – 11 gm%).
- Moderate (7 – 8% gm%)
- Severe (less than 7 gms%) iron deficiency anaemia.
- PCV less than 30%.
- Serum ferritin below 30 micro gm/l.
- Ethical committee approval was taken before start of study.
- A written informed consent was obtained from the patient who were willing to participate in the study.

Exclusion Criteria:

1. All other cases of anaemia like sickle cell anaemia, thalassemia, Aplastic anaemia, Megaloblastic anaemia.
2. Anaemia due to liver disease.
3. Anaemia due to kidney disease
4. Anaemia due to Cardiovascualr disease.
5. Anaemia due to immunological diseases like rheumatoid arthritise SLE etc.
6. Anaemia due to chronic infections like chronic malaria.
7. Anaemia associated with disease of respiratory system.
8. WHO grading of very severe anaemia (Hb level <4gm /dl).
9. Patient with history of allergy to parenteral iron therapy.
10. Patients with Antipartum Haemorrhage. Pregnancy induced Hypertension, Gestational Diabetes Mellitus.
11. Patients with twin pregnancy, polyhydramnios.
12. Patients with other medical disorders like chronic HTN, DM, Heart disease, Renal disease, Liver disease, immunological disease.

All patients were admitted to hospital

- Haemoglobin, serum ferritn and PCV, peripheral smear comment (PSC) was done on admission to the hospital.
- Repeat Haemoglobin, Serum ferritin and PCV level, PSC after 28 days of last dose of parenteral iron after calculated total dose infusion (TDI).
- Repeat Hemoglobin and PCV level at 38 weeks gestation to evaluate the status of anaemia before delivery.

Methods of Infusion: 200 mg of elemental iron diluted in 200 ml Normal saline is given as slow IV over 30 minutes and it is repeated on alternate days till TDI is completed. Maximum of 3 doses repeated per week.

Data was collected as per this table and data was analyzed by paired t TEST and P value less than 0.5 was taken in to consideration. Prior to IV iron therapy (admition), at 28 days after completion of iron therapy and at 38 week of gestation following data was collected like Hb%. PCV, Serum ferritin and peripheral smear comment.(Hb=hemoglobin, PCV=Packed cell volume)

Result

Among the total number of 104 patients studied, mean age of the study group was 25.4 ± 3.26 years. Teen age pregnancies with anaemia formed 5.7% of the study group. Most cases, i.e. 77.9% were between 20 – 30 years. Elderly gravidas comprised 16.4%. In the study group 59.6% were primigravida and 40.4% were multigravida.

Out of 104 patients, 62 patients (59.6%) were of gestational age < 28 weeks and 42 (40.4%) were > 28 weeks of gestational age. Majority of patients 77.9% belongs to low socio economic status with nutritional anaemia.

Table 1: Degree of Anaemia

Degree of Anaemia	Count	Percentage
Mild Anaemia (8-11 gm%)	46	44.2
Moderate Anaemia (7-7.9gm%)	20	19.2
Severe Anaemia (<7 gm%)	38	36.6
Total	104	100

From the above table, 44.2% belong to mild anaemia group, 19.2% belong to moderate and 36.6% patients belong to severe anaemic group. The mean Hb% on day of Admission was 7.670 gm% which raised to 10.388 on day 28 of completion of iron therapy. Thus the mean Hb rise on day 28 was 2.718 gm% which is statistically significant (p value being 0.000).The Hb level at 38 weeks of gestation is 9.162 which is significantly higher when compared with Hb value on the day of admission (p value being 0.000).

Table 2: Statistical analysis table for haemoglobin

Paired Samples Statistics

		Mean	N	Std. Deviation	Std. Error Mean
Pair 1	HB (ADM)	7.670192	104	1.4491966	0.1421054
	HB(28 D)	10.388462	104	1.1723603	.1149594
Pair 2	HB (ADM)	7.670192	104	1.4491966	.1421054
	HB (38W)	9.162500	104	1.2318734	.1207951

HB=haemoglobin, ADM=admission

Paired Samples Correlations

		N	Correlation	Sig.
Pair 1	HB (ADM) & HB (28 D)	104	0.631	0.000
Pair 2	HB(ADM) & HB (38W)	104	0.407	0.000

Paired Samples Test

	Paired Differences					t	Off	Sig.(2-tailed)
	Mean	Std. Deviation	Std. Error Mean	95% confidence interval of the Difference				
				Lower	Upper			
Pair 1: HB(ADM)-HB(28D)	-2.7182692	1.1532785	.1130883	-2.9425531	-2.4939853	-24.037	103	.000
Pair 2: HB(ADM)–HB (38W)	-1.4923077	1.4713901	.1442817	-1.7784564	-1.2061590	-10.343	103	.000

Table 3: Comparision of mean PCV values on admission Day, Day 28 of completion of iron therapy and at 38 weeks of gestation

Day	Mean PCV %
Day of Admission	22.335
Day-28 of Completion of Iron Therapy	30.352
38 weeks of Gestation	26.959

From the above table the mean PCV on the day of admission was 22.335% which raised to 30.352% after 28 days of completion of iron therapy. The rise was 8.017% which was statistically significant (p = 0.000). The mean PCV value at 38 weeks of gestation is 26.959% which is also significant when compared with mean PCV at admission.

Table 4: Statistical analysis table for PCV

Paired Samples Statistics

		Mean	N	Std. Deviation	Std. Error Mean
Pair	PCV (ADM)	22.335577	104	4.4214595	.4335598
	PCV(28V)	30.352885	104	3.3019840	.3237862
Pair 2	PCV(ADM)	22.335577	104	4.4214595	.4335598
	PCV(38W)	26.959615	104	3.2369385	.3174079

Paired Samples Correlations

		N	Correlation	Sig.
Pair 1	PCV (ADM) & PCV(28D)	104	.622	.000
Pair 2	PCV(ADM) & PCV(38W)	104	.500	0.000

Paired Samples Test

	Paired Differences					t	Off	Sig.(2-tailed)
	Mean	Std. Deviation	Std. Error Mean	95% confidence interval of the Difference				
				Lower	Upper			
Pair 1 : PCV(ADM)-PCV (28D)	-8.0173077	3.5044062	.343653	-8.6988273	-7.3357881	-23.331	103	.000
Pair 2 : PCV(ADM)-PCV(38W)	-4.6240385	3.9640985	.3887118	-5.3949567	-3.8531202	-11.896	103	.000

Table 5: Peripheral smear on admission day, day 28 of completion of iron therapy

Peripheral smear on day of admission

Type	Frequency	Percentage (%)
DA	36	34.6
MH	25	24
NH	30	28.8
NN	13	12.6
Total	104	100

DA=dimorphic anaemia, MH=microcytic hypochromic, NH=normocytic hypochromic, NN=Normocytic norchromic.

There was increase in normocytic normochromic patients after 28 days of completion of iron therapy. There is definite improvement of peripheral blood picture after iron therapy. The mean serum ferritin level at admission is 18.50micro gm/L which raised to 54.225 micro gm/L at 28 days after completion of iron therapy which is significant (P. value being 0.000).

Table 6: Statistical analysis table for serum ferritin

Paired Samples Statistics

		Mean	N	Std. Deviation	Std. Error Mean
Pair 1	S. Ferritin (ADM)	18.503846	104	6.61205032	.6483649
	S. Ferritin (28D)	54.225000	104	18.2951728	1.7939893

Paired Samples Correlations

		N	Correlation	Sig.
Pair 1	S. Ferritin (ADM) & S. Ferritin (28D)	104	.509	.000

Paired Samples Test

	Paired Differences					t	Off	Sig.(2-tailed)
	Mean	Std. Deviation	Std. Error Mean	95% confidence interval of the Difference				
				Lower	Upper			
Pair 1: S. Ferritin (ADM) – S. Ferritin (28D)	-35.721153	15.9765038	1.5666251	-38.828185	-32.614122	-23.331	103	.000

No significant adverse effect of the drug were noted. There were only few minor side effects observed. One patient developed mild hyper sensitivity reaction which was controlled by medication.

Discussion

In the present study, Iron sucrose was selected for therapeutic use in IV route. 200mg of iron sucrose was diluted in 200ml of NS and infused over 30 minutes without a test dose. Out of 119 patients 9 patients did not come for follow up and 6 patients delivered before 38 weeks. They are excluded from the study. In the present study majority of the patients were between the age group 20-30 years of age. In the previous studies, emphasis was not given on the gravidity, but in present study 59.6% were primigravida and 40.4% were multigravida, hence gravidity did not seen to affect the outcome. In the previous studies socioeconomic status was not taken in to account, but in the present study 77.9% of patient belongs to low socio economic status which implies that anemia affects more to low socio economic status group.[7]

In the previous studies, degree of anemia was not taken into account, but in the present study, patients belongs to Mild (44.25%), Moderate (19.2%) and severe (36.6%) anaemia groups and all the groups respond to injectable iron – sucrose. In our study comparison of mean haemoglobin on admission day was made with that on day 28th of completion of iron therapy and at 38 weeks of gestation. The results revealed that injectable iron sucrose therapy in pregnant anaemic women significantly raised the haemoglobin when compared admission day value (7.61gm%) with those on day 28 of (Mean = 10.338gm%) completion of therapy and at 38 weeks of gestation (Mean 9.162 gm%). p value being (0.000).This is as per the study of Dr. Nasir Khokar et al.[7]

Mean PCV values were compared between admission day, that on 28th day of completion of iron therapy and at 38 weeks of gestation. it was found that the mean packed cell volume raised significantly after parenteral iron sucrose therapy when compared admission day value (22.335%) with day 28 of completion of iron therapy (30.352%) and at 38 weeks of gestation (26.295%).p value being(0.000). Examination of peripheral smear on day of admission and on 28 day of completion of iron therapy revealed that there was increase in the normocytic normochronic patients after iron sucrose therapy. This implies that there is marked improvement in peripheral blood picture after iron sucrose therapy. This is as per the study of Wali et al (2002).[8]

In our study, comparison was made between mean serum ferritin level at admission and at 28 day after completion of iron therapy, it was found that mean serum ferritin level on the day of admission (18.503 micro gm /L) was raised to(54.225 microgram /L) on 28 day of completion of iron therapy and the rise was statistically significant (p = 0.000). This is as per the study of Breymann et al (2005).[9,10]

Earilier studies showed that patients receiving Iron dextran inj suffered from various adverse reactions and life threatening Anaphylactic reactions. But patients receiving iron-sucrose suffered very minimal adverse drug reactions during its administration.[11]

A study conducted by Hoigne et al.[12] compared the safety of iron sucrose with iron dextran and they found that not a single life threatening reaction was observed during 8100 patient years with approximately 160,000 ampoules of iron sucrose. Only in few situations minor drug reactions occurred. So they concluded that Iron – sucrose has a better safety profile.

In our study one patient developed hyper acidity, 2 patients arthralgia, 2 patients headache, 2 patients metallic taste, 2 patients chills and rigour.

Four patients developed pain at the injection site and two develop nausea and vomiting. Only one case developed mild hypersensitive reaction with dyspnoea which was controlled by inj. Hydrocortisone and inj. Pantoprazole. No severe adverse drug reaction was noted during the study period. This proves that iron sucrose injection is an effective and safe option for treating iron deficiency anaemia in pregnancy.

Conclusion

To conclude in our study "To study the Efficacy, safety and compliance of injectable iron-sucrose in pregnancy with mild, moderate and severe Anaemia" involving 104 pregnant women between 16 weeks to 32 weeks of gestation with mild, moderate and severe anaemia getting TDI it can be concluded that

- Injection iron sucrose is safe and effective in the management of anaemia in pregnancy with a better compliance.
- It has minimal side effects.
- It restores body iron faster.

- It raises hemoglobin at a faster rate.
- There is also remarkable improvement in other hematological parameters like PCV & PSC.

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