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THE EFFECT OF IRON SUPPLEMENTATION ON FETOMATERNAL OUTCOME: A PROSPECTIVE STUDY

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ABSTRACT

Anaemia is responsible for variable symptoms ranging from mild weakness to increased cardiac output leading to cardiac failure, increase incidence of preterm labour, preeclampsia, sepsis, and haemorrhage. It causes increased perinatal morbidity and mortality by causing premature deliveries, low birth weight babies and intra uterine growth retardation. The aim of this study was to estimate body iron stores (serum ferritin) in anaemic pregnant women, to evaluate the efficacy and side effect of iron supplementation regimen in anaemia of pregnancy and to study the effect of treatment on fetomaternal outcome. This propective study was conducted over a period of 12 months A total of 40 pregnant women consecutively reporting were recruited for this study. Study subjects were randomly allocated into two groups of 20 each one group receiving oral and another parentral therapy before and after treatment. We also compared the results of oral versus parenteral iron supplementation on the anaemia status of pregnant wome. In oral group mean age was 24.05 and in parenteral group mean age was 24. We found that parenteral iron is better than oral iron given to anaemic women mainly in second trimester of pregnancy to improve their iron stores but with 100% compliance fetomaternal outcome is comparable in both groups.

KEYWORDS: effect of iron, fetomaternal outcome, perinatal morbidity and mortality.

INTRODUCTION

Every year approximately 600000 women die from complications of pregnancy and childbirth.[1] According to The Federation of Obstetric and Gynaecological Societies of India (FOGSI) (1997) anaemia is responsible for 64.4% of maternal deaths in India.[2] Anaemia is responsible for variable symptoms ranging from mild weakness to increased cardiac output leading to cardiac failure, increase incidence of preterm labour (28.2%), preeclampsia (31.2%), sepsis and haemorrhage.[4] It causes increased perinatal morbidity and mortality by causing premature deliveries, low birth weight babies and intra uterine growth retardation.[5] It leads to low iron stores, iron deficiency anaemia and cognitive dysfunction in infant. The gross iron requirement in pregnancy is about 1240 mgs including obligate iron losses (230 mg), expansion of red cell mass (450 mg), transfer to foetus (250 mg), placenta and umbilical cord (90 mg), loss at delivery (200 mg). However amenorrhoea saves around 150 mg of iron and post partum decline in red cell mass saves another 450 mg of iron; so net requirement of pregnancy ranges from 2-4 mgs/day (absorbed iron), requiring dietary iron of 20-40 mg/day.[11] Food iron is present in most diets in a proportion of 6mg/ 1000 calories and is made up of heme and non heme iron. Factors inhibiting the absorption of iron include antacids, phosphates, phytates, tetracyclines, presence of food in the stomach etc.

Parenteral iron therapy is a safe and effective method of treatment of anaemia in hospital set up. It ensures more compliance but causes side effects like staining of skin at injection site injection abscess, arthralgia, fever, anaphylaxis etc. Oral iron causes intolerance evidenced by epigastric pain, vomiting and constipation but it is more convenient as an iron supplement.[9] In some studies of oral versus parenteral iron supplementation, not only were the side effects less and compliance better with parenteral iron haemoglobin; rise was also significantly higher than oral therapy. The aim of this study was to estimate body iron stores (serum ferritin) in anaemic pregnant women, to evaluate the efficacy and side effect of iron supplementation regimen in anaemia of pregnancy and to study the effect of treatment on fetomaternal outcome.

MATERIALS AND METHODS

This propective study was conducted in department of Obstetrics and Gynaecology, Himalayan Institute of Medical Science, Dehradun, over a period of 12 months with approval from Ethical committee and informed consent from subjects participating in the study. A total of 40 pregnant women consecutively reporting to

Gynaecology outpatient department were recruited for this study. Study subjects were randomly allocated into two groups of 20 each one group receiving oral and another parentral therapy before and after treatment.

Inclusion criteria

1) A gestational period of less than 36 weeks.
2) Moderate to severe anaemia (haemoglobin less than 10gm%) and
3) Patient willing for enrolment of study.

Exclusion criteria:

1) Medical disorders like tuberculosis, diabetes mellitus, chronic infections etc.
2) Patients of gestational age >36 weeks as they require blood transfusion for early improvement.

Study protocol

General examination was done which were followed by systemic examination and obstetric examination of all the pregnant women. About 8-10ml of venous blood was taken from the patient at the first visit for baseline values. It was divided into two parts; about 3 ml of blood was transferred to vacutainer containing EDTA solution which was sent to haemotology and biochemistry laboratory.

The parameters done with this sample were

Haemoglobin, Mean corpuscular volume, mean corpuscular haemoglobin, Mean corpuscular haemoglobin concentration, Peripheral smears was stained with leishman's stain to look for red blood cell morphology.

Test to be done in biochemistry laboratory

- Serum ferritin.
- Serum total iron binding capacity.

Blood samples were taken initially for baseline evaluation of blood indices and then near term to see the effect of iron supplementation in the two groups i.e. those receiving oral and parentral therapy respectively. The side effects of both parenteral and oral iron therapy were noted and patient having anaemia after being treated were evaluated in respect of maternal and fetal outcome.

Statistical Analysis

Interpretation and analysis of the obtained result in done using descriptive method i.e. in rates, ratios and proportions etc. Student t test and Chi square test was applied to ascertain statistical significance. Intravenous iron is given at the rate of 1 ml/ min, maximum dose being 100 mg by diluting 5 ml vial in 250 ml normal saline. Maximum 250 mg given not more than 3 times a week and is rarely associated with anaphylactic reaction and can also be given in patient undergoing haemodialysis as it has low molecular weight. In i.v group available as iron dextran, iron sucrose and ferrous gluconate iron dose calculated from formula: Body weight in kg x(desired Hb –patients Hb) x 2.21+ 1000mg.

1000mg was taken for complete restoration of stores in patients with continuous blood loss otherwise 500 mg is adequate. Intramuscular iron(available as iron dextran, iron sorbitol citrate complex) given as 1.5mg/kg bodyweight by Z technique single dose of not more than 2 ml containing 100 mg of iron is recommended (66).

RESULTS

The present study was conducted to compare the results of oral versus parenteral iron supplementation on the anaemia status of pregnant women, trying to ensure 100% compliance in both the group. In oral group mean age was 24.05 and in parenteral group mean age was 24. The difference in the mean age was not significant in the two groups. Mean gestational age in oral group was 19.65 and in parenteral was 20.65. The difference in gestational age at first visit was not significant in the two groups. The difference in the distribution of parity in the two groups was not significant statistically. [Table.1].

The literacy was comparable in the two groups [Table.2] Maximum patients were illiterate. Haemoglobin.

Hb = initial haemoglobin.

HbP = haemoglobin after supplementation.

The initial mean hemoglobin was comparable in the two groups of patients, after iron supplementation in both the groups, the final mean haemoglobins had no statistically significant difference. In this Student's t-test was used. After iron supplementation, the rise in haemoglobin in both oral and parenteral [Table.3]. The mean heamatocrit value remained comparable prior to supplementation and no statistically significant difference was demonstrated supplementation between the two groups [Table.4].

Mean Corpuscular Volume (MCV).

MCV= initial value.

MCVP= MCV after supplementation.

MCV values improved in both oral and parenteral group and it was statistically significant in parenteral group [Table.5].

Mean Corpuscular Haemoglobin Concentration (MCHC)

MCHC= initial value

MCHCP=MCHC after supplementation

Comparison of Mean Corpuscular Haemoglobin Concentration in oral and Parenteral groups before and after supplementation. Prior to supplementation, MCHC in the two groups was comparable. After treatment, parenteral group had better MCHC as compared to oral groups which was statistically significant; though, the mean value of MCHC had fallen slightly in both the groups. There was significant difference in the MCHC, before and after supplementation, however, showing a fall in the value. [Table.6].

Mean Corpuscular Haemoglobin (MCH)
MCH= initial value.
MCHP= MCH after supplementation.

Thus improvement in the MCH value after treatment was comparable in both the groups, with no statistical difference. Comparison of Mean Corpuscular Volume in oral and Parenteral groups before and after supplementation. After treatment with iron, oral or parenteral, there was no statistically significant improvement in both the groups [Table.7].

Serum ferritin
Ferritin = initial value.
FerritinP = Ferritin after supplementation.

Comparison of Serum Ferritin in oral and Parenteral group before and after supplementation. After iron supplementation, parenteral iron group showed a remarkable rise in serum ferritin as compared to oral, which was statistically highly significant [Table.8].

Serum Iron
Iron = initial value.

IronP = Iron after supplementation
Serum iron values showed statistically significant difference after treatment [Table.9].

Serum Total Iron Binding Capacity (TIBC)
TIBC=initial value.

TIBCP=TIBC after supplementation
There was a statistically significant fall in TIBC in Subjects who received parenteral iron: there was significant fall in oral group. In patients who had received oral iron, initial and final values of TIBC showed no statistical but patients who had received parenteral iron, showed a significant fall in total iron binding capacity, after treatment [Table.10].

Maximum number of babies of the treated mothers in both group had good birth weight. iron group, were statistically not significant [Table.11]. Maximum number of babies of the treated mothers in both group had good apgar score [Table.12]. One patient had anaphylaxis and was treated and discharged the next day.

Table-1: Parity distribution.

Parity	Oral	Parenteral	Total
Primipara	11	8	19
1st Gravida	0	2	2
2nd Gravida	6	7	13
3rd Gravida	2	3	5
4th Gravida	1	0	1
Total	20	20	40

Chi square = 3.75 p=0.440.

Table -2: Literacy status.

Literacy	Oral	Parenteral	Total
Illiterate	8	5	13
Primary	5	6	11
Secondary	6	6	12
Graduate	1	3	4
Total	20	20	40

Chi square =1.78 p=0.618.

Table -3: Comparison of haemoglobin in oral and parenteral group before and after treatment.

Haemoglobin	Subject	No.	Mean (gm%)	P-value
Hb	Oral	20	9.47±0.72	0.884
	Parenteral	20	9.50±0.57	
HbP	Oral	20	10.19±0.71	0.001
	Parenteral	20	11.24±0.80	

Table 4: Comparison of haematocrit in oral and parenteral group before and after treatment (n=20).

Haematocrit	Subject	No.	Mean	P-value
PCV	Oral	20	30.83±1.44	0.176
	Parenteral	20	30.16±1.63	
PCVP	Oral	20	35.66±2.72	0.950
	Parenteral	20	35.71±2.32	

Table 5: Comparison of mean corpuscular volume in oral and parenteral group before and after treatment.

Mean Corpuscular Volume	Subject	No.	Mean±SD	P-value
MCV	Oral	20	78.36±3.35	0.548
	Parenteral	20	78.95±2.85	
MCVP	Oral	20	84.08±2.44	0.001
	Parenteral	20	90.06±4.98	

Table- 6: Comparison of MCHC in oral and parenteral group before and after treatment.

Mean Corpuscular Haemoglobin Concentration	Subject	No.	Mean±SD	P-value
MCHC	Oral	20	30.92±1.59	0.778
	Parenteral	20	31.09±2.16	
MCHCP	Oral	20	32±2.86	0.009
	Parenteral	20	29.31±1.70	

Table 7: Comparison of Mean Corpuscular Haemoglobin in oral & Parenteral groups before and after supplementation.

Mean Corpuscular Haemoglobin	Subject	n	Mean (pg) ±SD	P-value
MCH	Oral	20	27.51±2.28	0.158
	Parenteral	20	26.30±2.99	
MCHP	Oral	20	28.71±2.82	0.826
	Parenteral	20	28.9±2.62	

Table- 8: Comparison of serum ferritin in oral & Parenteral groups before and after supplementation.

serum ferritin	Subject	n	Mean±SD (µg/It%)	P-value
Ferritin	Oral	20	9.29±0.70	0.216
	Parenteral	20	8.88±1.26	
ferritinP	Oral	20	15.88±2.19	0.001
	Parenteral	20	31.12±1.85	

Table 9: Comparison of serum iron in oral & Parenteral groups before and after supplementation.

serum iron	Subject	No.	Mean±SD (µmol/It)	P-value
Iron	Oral	20	31.87±5.73	0.293
	Parenteral	20	30.34±2.97	
IronP	Oral	20	33.48±4.89	0.025
	Parenteral	20	37.61±5.38	

Table 10: Comparison of TIBC in oral & Parenteral groups before and after supplementation.

Serum Total Iron Binding Capacity	Subject	No.	Mean±SD (µmol/It)	P-value
TIBC	Oral	20	124.56±6.59	0.991
	Parenteral	20	124.58±4.27	
TIBCP	Oral	20	130.61±5.91	0.001
	Parenteral	20	111.64±2.89	

Table 11: Birth weight.

Weight	Oral (n=20)		Parenteral (n=20)	
	No.	%	No.	%
< 2500 gm	3	15	2	10
≥ 2500 gm	17	85	18	90

Chi square = 0.23.
p = 0.632.

Table 12: Apgar score.

Apgar score	Oral (n=20)		Parenteral (n=20)	
	No.	%	No.	%
Normal (≥7)	18	90	19	95
Fairly low (4-6)	2	10	1	5
Critically low (≤3)	0	0	0	0

Chi square = 0.36.
p = 0.548.

Table- 13: Side effects of iron supplementation in oral group.

Side effect	Dyspepsia	constipation	Diarrhea	Vomiting	Generalized rashes and itching
No. of patients	10	5	3	2	1

Table- 15: Side-effects of Parenteral iron supplementation.

Side Effects	No.
Local pain	
Mild	5
Severe	1
Staining	
Mild	3
Moderate	1
Fever	1
Systemic ache	1
Arthralgia	2
Itching & rashes	1
Immediate headache & giddiness	1
Malaise	1
Vasovagal	1
Systemic reaction	1
Admission	1

DISCUSSION

According to National Family Health Survey 2005-06 anaemia prevalence is 57.9%.[14] This study was conducted because of high incidence of maternal mortality and morbidity due to anaemia especially in rural areas due to lack of medical facilities and untrained birth attendants. This hospital is a tertiary hospital getting referral patients from nearby hills, cities and towns. The direct causes of maternal deaths are IDA which continues to be the leading nutrient deficiency in the world, affecting the lives of billion persons, despite considerable efforts to decrerase its prevelance for past 3 decades.[3] Patients with initial haemoglobin between 8 and 11gm% were enrolled for the study. Initial haemoglobin of patients in our study, was between 8 and 11gm%. This ranges was chosen because haemoglobin rise was well demonstrated in this range; also, it is unethical to include patients of severe anaemia (Hb <7gm%) in such a trial. Though, Bhatt et al[11] has not given any such range in his study by Jenkinson et al[12], they have excluded patients with initial haemoglobin less than 10 gm%. Prema et al[13] included patients with haemoglobin between 5 and 8 gm% while Sood et al[14], took patients with initial haemoglobin >5gm%. Ideally patients with haemoglobin less than 8 gm% require admission and blood transfusion.

The present study comprise of two groups of patients; 20 patients were given 100 mg elemental iron per day orally along with folic acid 500 µg for 100 days and the other 20 patients were given, parenteral iron 250 mg each, at an interval of 4-6 weeks along with folic acid tablets. An initial deworming was done in all the patients. Patients in the two groups were comparable with respect to age, gestational age at first visit, parity and literacy status. In our study mean age of the subjects was 24.05 ± 3.72 years and 23.92 years in the oral and parenteral group respectively. Majority of the patients were primigravidas 40% in oral and 45% in parenteral group respectively. Mean initial haemoglobin of the oral group was 9.47±0.72gm% and of the parenteral group was 9.50±0.57gm%; there was no statistically significant difference. After treatment, mean haemoglobin in oral group was 10.19±0.71gm% and in parenteral group was 11.24±0.80 gm%. In both groups, the rise was statistically significant. Final mean haemoglobin in the two groups was comparable with no significant difference. Mean initial haematocrit in oral group was 30.83±1.44% and in parenteral group, 30.16±1.63%. There was no significant difference. Mean final haematocrit in oral group was 35.66±2.72gm% and in parenteral group was 35.71±2.32gm%. Thus supplementation improved haematocrit in both groups. Mean final haematocrit remained comparable in the two groups. Mean initial MCHC (mean corpuscular haemoglobin concentration) in oral group was 30.92±1.59% and in parenteral group, 31.09±2.16%. Which were comparable. Mean final MCHC in oral group was 32±2.86% and in parenteral group was 29.31±1.70%. mean final MCHC was significantly better in parenteral than oral group; the reason of fall in MCHC being increased mean corpuscular volume after iron supplementation, due to triggering of erythropoiesis. Mean initial MCH in oral group was 27.51±2.28 pg and in parenteral group 26.30±2.99 pg which were comparable. Mean final MCH in oral group was 28.71±2.82 pg and in parenteral group 28.9±2.62 pg. thus, no significant improvement occurred in both groups after supplementation; mean final value were comparable in the two groups. Initial MCV is oral group was 78.36±3.35 fl and in parenteral group, it was 78.95±2.85 fl which were comparable. Final mean MCV of oral

group was 84.03±2.44 fl. Mean final MCV of parenteral group was 90.06±4.98 fl. Thus, supplementation improved MCV in both the groups significantly. Rise in oral group was better than parenteral group.

Initial mean serum ferritin in oral group was 9.29±0.70 µgm/lt and in parenteral group 8.88±1.26 fl which were comparable. Final mean ferritin of oral group was 15.88±2.11 µgm/lt and in parenteral group, 31.12± 1.85 µgm/lt. Thus, supplementation improved serum ferritin in both the groups significantly. Rise was remarkably better in parenteral group. Initial mean serum iron in oral group was 31.87±5.73 µmol/lt and in parenteral group, 30.34±2.97 µmol/lt. Final mean serum iron was 33.48±4.89 µmol/lt in oral and 37.61±5.38 µmol/It in parenteral group. Thus, serum iron values showed statistically significant differences after treatment. Initial mean TIBC in oral group was 124.56±6.59 µmol/lt and in parenteral group, 124.58±4.27 µmol/It. Final mean TIBC in oral group was 130.61±5.91µmol/It and in parenteral group 111.64± 2.89 µmol/It.

Thus a statistically significant fall in TIBC occurred in subjects who received parenteral iron; there was no fall in oral group. The incidence of preterm deliveries was comparable in the two groups. The mean birth weight in oral group was 2731.37±475.235 gms and in parenteral group was 2786.63±435.581 gms. It was comparable with no statistically significant difference. Similarly the Apgar of infants in oral group was comparable to infant in parenteral group being 90% and 95%. The side effects of oral iron were dyspepsia, constipation, diarrhoea, vomiting, itching and rashes, which were tolerable.

The commonest side-effects with parenteral iron were local site pain and staining; the other side effects were fever, systemic ache, arthralgia, malaise, immediate headache and giddiness, itching and rashes. One patient had vasovagal attack of injection which was immediately managed. One systemic anaphylaxis was noted and patient was admitted. Two other patients required admission due to severe arthralgia, body ache and fever. No abscess or occurred. Majority of patients tolerated parenteral iron well. It is concluded that iron supplementation, oral or parenteral leads to definite improvement in all the blood parameters of iron status, during pregnancy. The main problem with oral iron supplementation is of compliance which is poor. Parenteral iron is a good substitute, to meet the iron requirements in pregnancy. Parenteral iron is also associated with side-effects but majority of patients tolerate it well. It can be given on the OPD basis under supervision, after the initial test dose and explaining the various side effects to the patients. Finally, it is concluded that parenteral iron is better than oral iron in anaemia in pregnancy.

CONCLUSION

Iron supplementation, oral or parenteral leads to definite improvement in all the blood parameters of iron status, during pregnancy thereby improving fetomaternal outcome in the form of good birth weight and apgar score. Parenteral iron is a good substitute, to meet the iron requirements in pregnancy. It can be clubbed with tetanus toxoid vaccine, which is quite popular, to ensure good compliance. Iron supplmenetation leads to improved fetomaternal outcome. Oral iron supplementation is associated with gastrointestinal side effects leading to non compliance but if 100% compliance is ensured then results of oral and parenteral iron supplementation. Oral iron was associated with mainly gastrointestinal side-effect Parenteral iron is associated with side-effects mainly fever and pain at the site of injection, but majority of patients tolerate it well. It can be given on the OPD basis under supervision, after the initial test dose and explaining the various side effects to the patients. Serum ferritin, which is the best indicator of iron status in the body rose remarkably after parenteral iron supplementation as compared to oral iron supplementation, thus proving the efficacy of the former. Finally, it is concluded that parenteral iron is better than oral iron given to anaemic women mainly in second trimester of pregnancy to improve their iron stores but with 100% compliance fetomaternal outcome is comparable in both groups.

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