Evaluation of Oral and Parenteral Iron Treatment Preparations in Pregnant Women with Iron Deficiency Anemia

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Abstract: Objectives: to evaluate efficacy and safety of oral and parenteral iron preparations in pregnant women with iron deficiency anemia. **Subjects and Methods:** this clinical trial completed Between August 2015 and December 2016, at Department of Obstetrics and Gynecology in Quesna Emergency Hospital in the wake of acquiring an endorsement of its institutional board audit. The review members are 121 pregnant ladies (mean age 25.5 years; extend 20 to 40 years), (mean GA 24 weeks; rang 16 to 28 weeks) who go to the obstetric outpatient facility for antenatal care with the conclusion of iron inadequacy Anemia. **Results**: From the results it can be concluded that parenteral iron more powerful than oral iron and the term of treatment was less in parenteral group. In our study oral iron preparation demonstrates a similar outcome toward the finish of the review however iron poly maltose complex shows more GIT up sets more than ferrous sulfate. Parenteral iron poly maltose complex shows huge augmentation in Hb, serum iron and serum ferritin yet this outcome switched toward the finish of the study and iron sucrose turn out to be more powerful. From the results it can be concluded that parenteral iron more powerful than oral iron and the term of treatment was less in parenteral group. **Conclusion**: From the results it can be concluded that parenteral iron treatment was better endured with higher increment in mean hemoglobin when contrasted with oral iron treatment. There were no genuine reactions with parentraliorn therapy. Parentraliorn therapy is a good substitute to oral iron therapy in moderate to severe anemia.

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1. Introduction:

Iron deficiency is an indication of element process**(1).** Pregnancy can bring about a condition of plethora, at the end of the day, the aggregate volume of blood is expanded by weakening and hemoglobin is thus decreased, periodically as low as 80%. Levels underneath this are neurotic, and the point is to raise the hemoglobin to at least 80%, if conceivable before conveyance. The most widely recognized wellspring of inconvenience in pale pregnancy is deficient ingestion of iron. The ordinary every day prerequisite for the pregnant lady is around 20mg of iron, even in cases in which the iron stores have not endured exhaustion before pregnancy, prompts to overwhelming requests upon maternal iron and normal fetal necessities add up to around 375mg. The edge between the patient's necessities and the amount of iron typically accessible in a decent eating regimen is an extremely limit one; indeed, the normal eating routine sometimes contains more than around 15mg a day. Of the aggregate sum of iron in nourishment, just around (10%) is accessible for retention. In this way, press treatment is required in these ladies**(2).**

WHO prescribed that, two billion individuals (>30% of the total population) are anemic, generally because of iron insufficiency, it is likewise the commonest therapeutic issue in pregnancy **(3)**.

The iron necessities increment during pregnancy, as in the third trimester, pregnant female needs six circumstances more iron than non pregnant female**(4)**.

WHO suggests that the HB fixation estimation of a base 11.0gm% amid pregnancy is typical**(5).**

Oral and parenteral iron preparations are utilized as a part of treatment and prophylaxis of iron insufficiency anemia**(6).**

Oral iron preparations are utilized to treat mild to moderate iron inadequacy anemia, however parenteral iron apreparations are utilized to treat severe iron deficiency anemia, bigotry to oral iron preparations and malabsorption**(7)**.

Objectives: to evaluate efficacy and safety of oral and parenteral iron preparations in pregnant women with iron deficiency anemia.

2. Subjects and Methods

This clinical trial completed Between August 2015 and December 2016, at Department of Obstetrics

and Gynecology in Quesna Emergency Hospital after obtaining an approval of its institutional board review. The review members are 121 pregnant ladies (mean age 25.5 years; run 20 to 40 years), (mean GA 24 weeks; rang 16 to 28 weeks) who go to the obstetric outpatient center for antenatal care with the determination of iron insufficiency sickliness 28 patients had been dropped out. Some of them had not finished the subsequent Others had not finish the decided treatment Only 121 ladies for who finish data were accessible with respect to clinical analysis and entire data were incorporated into this study.

Claculation of sample size

According to research work carried by **Panchal et al.,** the parenteral iron treatment had led to 57% increment of baseline haemoglobin level versus 38% increment after oral iron treatment for 12 weeks. Accordingly, at α=0.05 with a study power of 80%, a total sample size of 110 patients will be required but the addition of possible drop out rate (10%) will increase it to 121 cases**(8)**.

An informed consent acquired from enlisted members before start of the study. **The study cohort includes two groups:**

Group I (oral iron treatment group): had to fulfill the inclusion criteria:

Pregnant ladies with hemoglobin range: > 7gm/dl and under 10gm/dl. This group had gotten 200 mg of natural iron every day but after being randomized into two different oral iron treatment preparations subgroups; ferric hydroxide polymaltose complex or ferrous sulfate.

Randomization for subgroups of oral iron treatment amass as indicated by a produced task succession through utilizing measurable reading material irregular number table. The task succession conveyed in thus orchestrated misty shut envelopes. Every envelope contains a solitary treatment alternative.

Group II (parenteral iron treatment group): had to fulfill the inclusion criteria

Pregnant ladies with hemoglobin ≤ 7 g/dl randomized into two diverse parenteral iron treatment preparations subgroups; iron sucrose or ferric hydroxide polymaltose complex. Add up to measurement of parentally administrated iron sucrose or ferric hydroxide polymaltose complex incorporates the measure of iron expected to right hemoglobin shortage and recharge iron stores.

The aggregate dosage of iron is computed by the accompanying equation: Body eight (kg) × 2.3 × (Target Hb level - Patient's Hb) + 500mg (for stores). Randomization for subgroups of parenteral iron treatment gather as per a created task grouping by means of utilizing factual reading material arbitrary number table. The task grouping dispersed in subsequently orchestrated dark shut envelopes. Every envelope contains a solitary treatment choice.

Incorporation Criteria in the study were Age 20 – 40 years, Gestational age extend from 16 to 28 weeks, Singleton pregnancy and Rejection Criteria were Patients with known hypersensitivity to iron preparations, Patients with related diabetes mellitus or potentially hypertension, Patients with known hyperthyroidism or hypothyroidism, Patient with severe concurrent illness (cardiovascular, renal or hepatic disorders), Patients with a history of anemia due to any other causes such as, chronic blood loss, vitamin B12 deficiency, hemolytic anemia and bone marrow depression, Patients with haemochromatosis or other iron storage disorders, Transfused blood or blood products in previous two months, Previous intake of iron preparations which will be used in the study.

Statistical Analysis

Data were collected and entered to the computer using SPSS (Statistical Package for Social Science) version 20 Chicago, Inc, Illinose, program for statistical analysis. Data were entered as numerical or categorical, as appropriate. Quantitative data were shown as mean and SD. Independent sample t-test and Mann-Whitney U test were done to compare means and SD of 2 sets of quantitative data as appropriate. Fisher exact test and Pearson chi-square test were done to measure the association between qualitative data as appropriate. P (probability) value considered to be of statistical significance if it is less than 0.05.

3. Result:

The Hb, MCV, serum iron and ferritin at time of consideration were altogether higher in the oral group than the parenteral group. Interestingly the GA was essentially higher in the parenteral group (P<0.001 and < 0.002), while there was no critical contrast as respect the age, body weight and the parity (P =0.689, 0.390 and 0.489) **(Table 1**).

The Hb level was significantly higher in the oral group than the parentral group after 2 weeks,1 month and 2months respectively of beginning of treatment (P <0.001, < 0.001, 0.071)which may be due to the initial high level of Hb at time of inclusion in the oral group, with significant reversion of the condition after and 3 months with higher level in the parentral group (P <0.002). Concerning the serum iron, it was significantly higher in parenteral group all through the period of treatment (P<0.001, <0.003 and <0.001) In contrast to the serum ferritin which was higher in the oral group all through the period of treatment (P <0.001) **(Table 2).**

The side effects of oral and parenteral iron therapy. Constipation and metallic taste were significantly higher in the oral group while rashes,

hypotension, arthralgia, malaise and bluish discoloration at injection site were significantly higher in the parenteral group (P < 0.040, <0.20, <0.014, <0.014 and <0.014) **(Table 3).**

There was no significant difference between the oral and parenteral groups as regarding the patient compliance and satisfaction (P=0.729 and 1.0) **(Table 4).**

Table 1: Demographics of iron therapy groups.

	Oral N=91	Parenteral N=30	Independent sample t-test	*P*-value
	Mean± SD	Mean± SD		
Age (years)	25.5±3.7	25.9±4.2	0.403	0. 689
Weight (kg)	75.9±12.1	78.5±14.3	0.948	0.390
GA at time of inclusion (weeks)	24.49±2.65	26.1±1.5	3.195	0.002*
Hb (gm/dl) at time of inclusion	8.5±0.7	6.4±0.35	15.2	<0.001**
MCV at time of inclusion	59.6±6.9	40.6±3.1	14.5	<0.001**
Serum iron at time of inclusion (Pg/ml)	43.5±4.5	33.9±1.9	11.3	<0.001**
Serum ferritin at time of inclusion (Pg/ml)	38.8±4.1	30.3±1.2	11.16	<0.001**
Parity at time of inclusion: nullipara 1 2 3 4	33(36.3%) 23(25.3%) 22(24.2%) 12(13.2%) 1(1.1%)	11 (36.8%) 7(23.3%) 4(13.3%) 7(23.3%) 1(3.3%)	3.8®	0.401

® Fisher Exact test * Significant statistical difference ** High significant statistical difference

Table 2: The Haemoglobin, serum iron and ferritin after 2 weeks, 1 month, 2 months and 3 months in the oral and parentral groups

		Oral	Parentral	Independent sample t-test	*P*-value
		Mean± SD	Mean± SD		
Hb after 2weeks		8.91±0.56	7.38±0.59	12.7	<0.001**
Hb (gm/dl)	after 1month	9.27±0.57	8.47±0.72	6.2	<0.001**
Hb (gm/dl)	after 2 months	9.77±0.61	10.07±0.81	1.8	0.071
Hb (gm/dl)	after 3 months	10.51±0.69	11.01±0.82	3.2	0.002*
Serum iron(pg/ml)	after 1month	51.72±9.05	60.09±12.22	3.4	0.001*
Serum iron(pg/ml)	after 2 months	61.92±12.26	69.91±13.33	3.03	0.003*
Serum iron(pg/ml)	after 3 months	74.60±11.59	83.56±13.91	3.40	0.001*
Serum ferritin (pg/ml)	after 1month	114.21±39.15	64.20±5.20	Z=7.6	<0.001**
Serum ferritin(pg/ml)	after 2 months	123.76±48.10	49.74±7.96	Z=7.9	<0.001**
Serum ferritin(pg/ml)	after 3 months	116.66±45.55	62.80±13.86	Z=7.3	<0.001**

* Significant statistical difference ** High significant statistical difference Z (Mann-Whitney U test)

Table 3: The side effects of iron therapy in both groups

Side effects	Medication started		Fisher's exacttest	P-value
	Oral N=91	Parentral N=30		
Constipation	18(19.8%)	1(3.3%)	4.61	0.040*
Diarrhea	7(7.7%)	0(0.0%)	2.45	0.191
GIT upset (nausea, vomiting or Epigastric distress)	25(27.5%)	7(23.3%)	#0.20	0.655
Metallic taste	14(15.4%)	0(0.0%)	5.22	0.020*
Rash	0(0.0%)	2(6.7%)	6.17	0.059
Hypotension	0(0.0%)	3(10.0%)	9.331	0.014*
Headache	2(2.2%)	0(0.0%)	0.67	1.0
Arthralgia	0(0.0%)	3(10.0%)	9.331	0.014*
Bodyache	0(0.0%)	1(3.3%)	3.06	0.247
Malaise	0(0.0%)	3(10.0%)	9.331	0.014*
Injection site: Abscess Bluish discoloration	 0(0%) 0(0%)	 0(0%) 8 (26.7%)	 ---	 ----

* Significant statistical difference ** High significant statistical difference #X^2(Pearson chi-square)

Table 4: Patient compliance and satisfaction in the oral and parenteral groups

		Medication Started		Fisher's Exact Test	P-Value
		Oral N=91	Parenteral N=30		
Patient Compliance	Compliant	82(90.1%)	28(93.3%)	0.284	0.729
	Not Compliant	9(9.9%)	2(6.7%)		
Patient Satisfaction	Satisfied	81 (89.0%)	27 (90.0%)	0.02	1.0
	Not Satisfied	10(11.0%)	3(10.0%)		

4. Discussion:

In our study, the adequacy, wellbeing and bearableness of parenteral iron in treating pregnancy iron inadequacy anemia was contrasted with oral iron treatment. Parenteral iron is sheltered in pregnancy. It remedies anemia at brief span and renews iron stores superior to oral iron. This has been the perception in different studies as well **(9).**

Comparison with different studies is troublesome on account of various shorts utilized for lab parameters. Oral iron preparations utilized are likewise unique. As the rate of increment in hemoglobin is speedier, parenteral iron is reasonable for treatment of iron inadequacy anemia with lower hemoglobin in the third trimester. There was a very huge contrast in the ferritin level after treatment between the two groups, with iron stores reestablished just in the parenteral iron groups, which has likewise been seen by Bayoumeu et al., increment in ferritin is not a result of direct intravenous infusion of iron complex; rather, it is on account of the IVIS complex discharges iron quickly to endogenous iron restricting proteins with no testimony in the parenchymal tissue. It has a half-existence of around 6 h (10).

This is preference of IVIS over iron dextran or iron gluconate. Our study demonstrated the treatment results of aggregate 121 pregnant ladies treated with oral iron polymaltose complex, ferrous sulfate and parenteral iron sucrose and parenteral iron polymaltose complex for three months.

In this study we could contrast iron sucrose and other parenteral iron preparation and could look at the oral preparations. Following 3 months of development, every one of the 121 patients stayed on treatment without any passings or drop outs or different genuine symptoms, for example, anaphylactic shock. Three months treatment demonstrated that all patients had standardized hematological parameters (hemoglobin, anemia indices and serum ferritin and serum iron) with clinical change, giving 100% treatment accomplishment with every one of the four iron preparations.

In our study oral iron preparation demonstrates a similar outcome toward the finish of the review however iron poly maltose complex shows more GIT up sets more than ferrous sulfate. Parenteral iron poly maltose complex shows huge augmentation in Hb, serum iron and serum ferritin yet this outcome switched toward the finish of the review and iron sucrose turn out to be more powerful.

From the results it can be concluded that parenteral iron more powerful than oral iron and the term of treatment was less in parenteral group.

A few studies concur and some can't help contradicting our study. A Cochrane audit additionally found that intravenous iron medicines create a superior hematological reaction than oral iron and a speedier renewal of body iron stores**(11).**

Fundamentally increment in serum ferritin with parenteral administrationof iron than with oral administration is essential for rectification of anemia in pregnancy, particularly in patients withmalnutrition and rehashed pregnancies at short interims. The satisfactory iron stores are likewise critical amid lactation and for future pregnancies.

Serum ferritin has been viewed as the best quality level in building up iron insufficiency, with by and large acknowledged cut off level of 15 ng/mL, beneath which press stores are thought to be exhausted**(12).**

Both the groups showed considerable lessening in serum ferritin fixation, demonstrating consumption of iron stores. Ragip et al. demonstrated that the ascent in serum ferritin at day 28 was 5 ± 2.2 to 11 ± 11 lg/L (lg/L = ng/mL) in the oral group when contrasted with the I/V bunch where serum ferritin ascended from 1.4 ± 2.5 to 28 ± 26 lg/L at fourth week **(13).**

Bayoumeu et al. additionally saw a to a great degree huge contrast in the ferritin levels on day 30 between the two groups with iron stores reestablished just in the I/V bunch and a critical distinction was likewise seen at the season of conveyance between the two groups.

In the study by Al-Momen et al. it was found that serum ferritin ascended from 11.9 ± 5.0 to 5.95 ± 1.38 lg/L more than 6.9 ± 1.8 weeks in the I/V sucrose

aggregate and from 12.0 ± 5.3 to 52.4 ± 3.1 lg/L more than 9.14 ± 1.3 weeks in the oral group(13).

The higher incentive on day 7 and 14 in the IV group demonstrates that the reaction begins prior with intravenous iron sucrose has an unpredictable ingestion and is related with poor consistence. A few impacts of pregnancy—queasiness, regurgitating, motility issue with reflux esophagitis, acid reflux, propensity to hemorrhoids illness make the resistance to oral iron significantly more troublesome. The greater part of the symptoms in the oral gathering were gastrointestinal, which settled with further measurements. Despite the fact that none ceased the treatment, 9.9 % resistance was noted in the oral gathering. Be that as it may, Iron Sucrose was all around endured with no major unfavorable impacts in our study. The vast majority of the indications were mellow and no patient ceased the medicine**(14).**

Gastrointestinal symptoms were around 27.5% in the OI bunch, while the revealed occurrence differed from insignificant to 31% in different reviews. Al RA et al **(9).**

Mellow antagonistic occasions noted in the IVIS group were vomiting, rashes and giddiness after first dose of iron sucrose. Different studies revealed unsavory taste and fever, which were not seen in the present study. Bayoumeu et al; Because there were no genuine antagonistic medication responses and no scenes of hypersensitivity, we feel that it is ok for anemia in pregnancy(14).

The upside of iron sucrose is that dissimilar to iron dextran, it doesn't require a test dosage before administration. Anaphylactic responses are for the most part obscure with Iron Sucrose, the detailed frequency being 0.002 % **(10).**

This obviously infers by accomplishing target hemoglobin levels at the season of conveyance, requirement for blood transfusion in the peripartum period because of haemorrhage naturally decreases Many Indian reviews have utilized the intramuscular course for parenteral iron and announced symptoms, for example, pain, recoloring at infusion site and arthralgia. IVIS can't be given intramuscularly and does not have these symptoms**.(16).**

The impediments of this study were that albeit parenteral iron expanded serum ferritin altogether, patients were not followed-up in the post-natal period to figure out if hemoglobin levels were kept up amid lactation due to higher stores. We didn't rehash serum ferritin toward the finish of pregnancy nor amid the post-natal registration to perceive to what extent the stores last and the study populations were inadequate and necessities to expand the quantity of members to get more accurate outcomes.

5. Conclusion:

From the results it can be concluded that parenteral iron treatment was better endured with higher increment in mean hemoglobin when contrasted with oral iron treatment. There were no genuine reactions with parentraliorn therapy. parentraliorn therapy is a good substitute to oral iron therapy in moderate to severe anemia.

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