International Journal of Healthcare Sciences ISSN 2348-5728 (Online)
Vol. 3, Issue 1, pp: (315-322), Month: April 2015 - September 2015, Available at: www.researchpublish.com

A Comparative Study- Efficacy and Safety of Intravenous Iron Sucrose & Intramuscular Iron Sorbitol in Iron Deficiency Anemia during Pregnancies in Low Socio Economic Status

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Abstract: **Most women are not able to develop adequate iron stores during growth period. Thus women enter pregnancy state with depleted iron stores. This is a prospective Randomized controlled study conducted on women in the 2nd & early 3rd trimester of pregnancy with iron deficiency anaemia The mean age group in this study is 22.9±3.7 yrs, 43.33% of them were primigravida's & 56.7% of them were multigravida's. In iron Sorbitol group the mean rise in Hb% was by 0.8+0.17gm% at 4wks & 1.72±0.5gm% at delivery. Mean reticulocyte count by 0.46±0.14% & mean hematocrit rise was by 3.5±2.3% at 4wks & by 4.1±2.2% at delivery. In iron Sucrose group the rise in mean Hb% was by 2.2±0.4gm% at 4wks & by 3.04±0.5 gm% at delivery. Mean reticulocyte count by 0.46±0.15% & increase in mean hematocrit was 6.2±2.2% at 4wks & 6.9±2.9% at delivery. In group A the mean rise in ferritin level was 72.6±10.5 5ug/l & in Group B it was 31.6±5.2ug/l. In cases of iron Sorbitol 13.33% of the cases had severe reactions amounting to stop the injections & 60% had mild to moderate reactions continuing the injections. None of them developed severe reactions in Group A to stop the injections. The rise in parameters is statistically significant in both groups. Even though Iron Sorbtol is as efficacious as Iron sucrose in raising the Hb level, the Occurrence of more number of reactions restricts its use for intramuscular use. Iron Sucrose can be used as Observed Therapy ensuring definitive iron replenishment.**

Keywords: **Anaemia, Iron Sucrose, Parenteral Iron.**

1. INTRODUCTION

An estimated 60% of pregnant women in developing countries have anaemia. 40% of maternal deaths in the third world are related to anaemia. Nearly half of the global total number of anaemic women live in Indian subcontinent and in India alone the prevalence of anaemia during pregnancy may be as high as 88%[1].

Foetal iron metabolism is completely depended on maternal iron delivery, i.e., iron transport from the mother across the placenta. Placental transferring receptors play a key role in binding circulating transferring, which releases incorporated iron on the placental side. Supplementation with Iron/zinc and folic acid enhances placental superoxide dismutase activity, which scavenges superoxide radicals and protects the foetus from their deleterious effects. Women with a haemoglobin level below 9g/dl are at increased risk for prematurity, small for gestational age babies and spontaneous abortions. According to World Health Organisation (WHO), oral iron programs have often failed to reduce frequency of iron deficiency anaemia. High levels of iron deficiency anaemia exist in pregnancy despite routine use of iron prophylaxis adopted by many centres in the developing world. The WHO technical working group on the prevention and the treatment of severe anaemia has documented that parenteral iron therapy produces a rapid and complete correction of iron

deficiency, including replacement of iron stores producing a more rapid erythropoietic response than oral iron replacement. Anaemia during pregnancy and its management remains an important issue in perinatal medicine. Correct diagnosis and treatment lead to effective management of foetal and maternal risks and improved perinatal outcome[2].

There are several studies on use of parenteral iron in pregnancy. Cost factor & occurrence of anaphylactoid reactions preclude their routine use in clinical practice. The main Objective of our study was to determine an alternative iron supplementation with better efficacy, compliance, and safety in treatment of iron deficiency anaemia during pregnancy and puerperium & to reduce blood transfusions during pregnancy & labour.

Hence, this study was undertaken to evaluate the measures & overcome these disadvantages. So in present study we have evaluated the efficacy of iron sorbitol with iron sucrose.

2. MATERIALS AND METHODS

The study titled "A Comparative study: Efficacy, Safety, & Compliance of intravenous Iron Sucrose & Intramusclar Iron Sorbitol in Iron Deficiency anemia during Pregnancy'' was conducted in the Department of Obstetrics & Gynecology of Yenepoya Medical College Hospital, Deralakatte, Mangalore during two years period.

A total of 60 women included in the study group.

Inclusion Criteria:

- Patient should be in II nd or early III rd trimester.
- Patient should not be on any modality of treatment for anaemia during the period of study.
- All diagnosed cases of Iron deficiency anaemia in pregnancy with haemoglobin levels 7gm% to 9gm%
- Willing for the parenteral therapy
- Likely to come for follow up.
- Patient having oral iron intolerance

Exclusion Criteria:

- Patients with anaemia not attributable to Iron deficiency.
- Pregnancy with history of Asthma, Eczema and other atopic allergy.
- Known hypersensitivity to parenteral iron.
- Patients with iron overload or disturbance in utilization of iron.
- Patients in first trimester.
- Pregnancy with severe anaemia with medical disorder like diabetics mellitus, hypertensive disorder of pregnancy

The patients attending the outpatient were selected for the study and after explain in detail about the study design a written consent was taken from the patient & then were included in the study. A thorough history was elicited from those women chosen for study. All the study subjects were analyzed in full details regarding age, literacy, socioeconomic status, diet, and parity. Pregnancy details regarding ANC, significant past and family history, Diet history were noted. Subjects were followed further by a thorough General Physical, Systemic and obstetric examinations. These women were admitted to the hospital & their complete haemogram, serum ferritin were done & total iron requirement was calculated using the formula given below.

2.4 X Body weight in kg x Hb deficit in gm%= gms of iron+ (500gms during pregnancy)

Visit I:

The patients were then randomly selected into those going to receive iron sorbitol & those who were to receive iron sucrose.

Group A: Consisted of women who were randomized to receive parenteral Iron Sucrose preparation.

Group B: consisted of women who were randomized to receive parenteral Iron Sorbitol preparation.

After detailed evaluation with adequate precaution the parenteral iron infusion was done.

- Iron Sorbitol: the total dose required was calculated. After giving the test dose, patient was observed for 15-30 min for appearance of any signs & symptoms of hypersensitivity reaction. If there is no reaction then the injections are given daily or on alternate days in doses of 2 ml intramuscularly.

Adverse reaction monitoring:

No direct leading questions were asked to elicit side effect. No check list for any specific side effects was provided. Only those side effects volunteered by the patient was recorded & discontinuation of treatment considered..

- Iron Sucrose: the dosage of iron sucrose is expressed in terms of mg of elemental iron. Each ml contains 20mg of elemental iron. The total dose required was calculated. No test dose was given. 100-200mg of iron sucrose administered as slow i.v bolus injection over a period of 10-15 minutes. Repeated every alternate day or three times a week. If there were any adverse reaction then injections were stopped & treated. The patient was discharged after bolus injections of total dose & advised to come for follow up.

Visit II:

The patients were examined again mainly looked out for general condition & the complete hemogram & serum ferritin levels were repeated after 4wks of administering the drug. The results were compared with complete hemogram & serum ferritin reports before administering the drug & relative efficacy of the two drugs were compared.

Visit III:

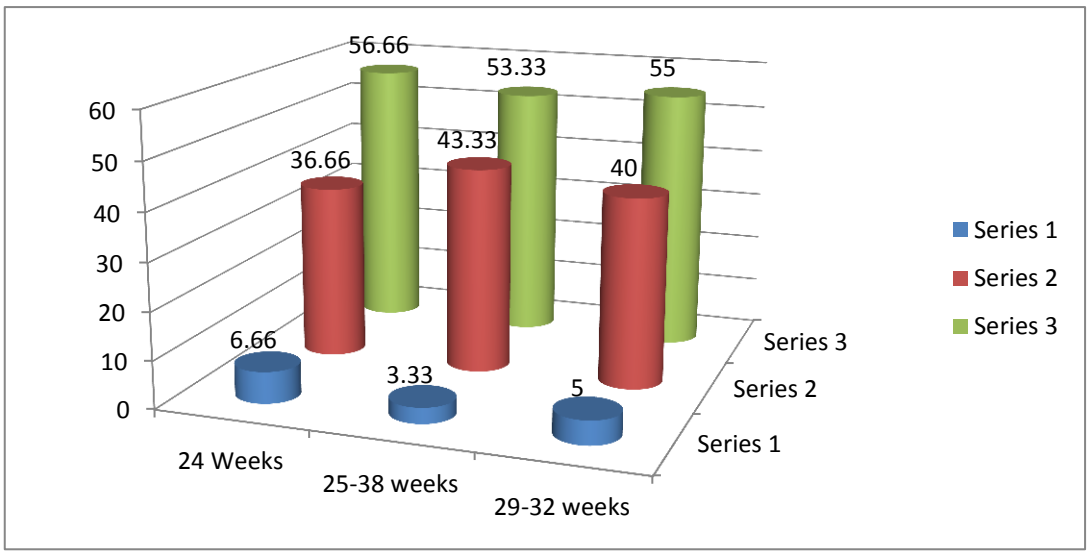
The patients were examined again just before delivery for general condition & the haemoglobin & the haematocrit levels were repeated. The results & the relative efficacy of both the drugs were compared.

3. RESULTS

Table 1: Gestation age in weeks between two groups

Gestation age in weeks	Group A (n=30)		Group B (n=30)		Combined (n=60)	
	No.	%	No.	%	No.	%
<24 weeks	2	6.66	1	3.33	3	5
25-38 weeks	11	36.66	13	43.33	24	40
29-32 weeks	17	56.66	16	53.33	33	55

Gestational Age:



This Table shows the distribution of cases studied according to their gestational age. As the study was done on cases who are in their second trimesters & early 3rd trimesters, 55% of them were of 29-32wks of gestation, 40% of the cases were of 25-28 wks & rest 5% were of <24 wks.

Table 2: Comparison of investigations before and after parenteral iron between two groups of cases studied.

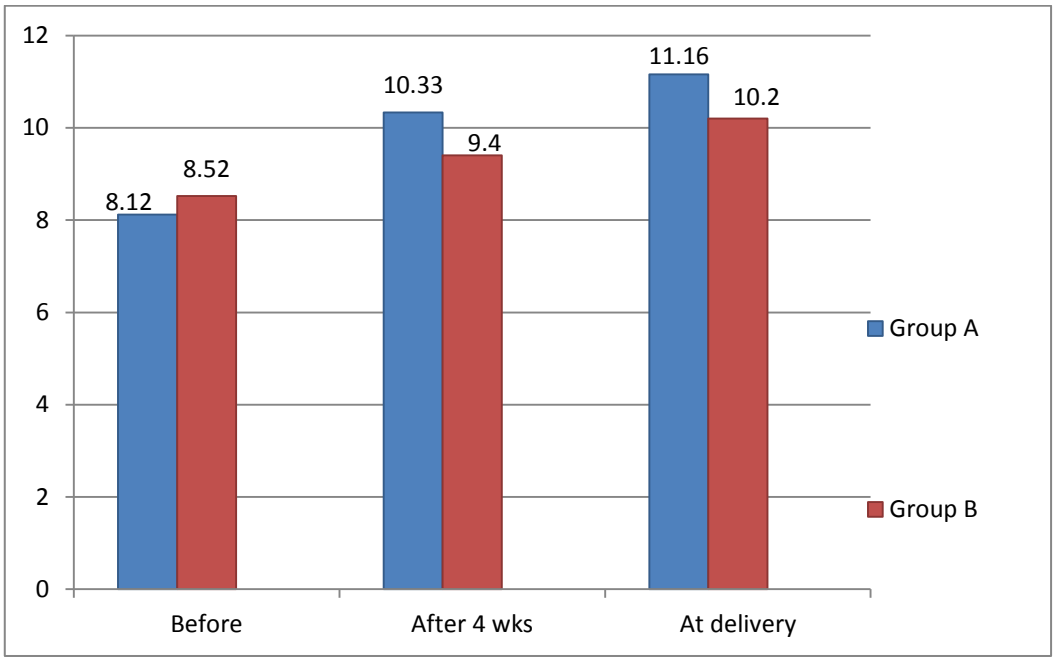
Investigations		Group A	Group B
Hemoglobin	Before	8.13 ±0.35	8.52 ±0.22
	After 4 wks	10.33 ±0.34	9.4 ±0.24
	At Delivery	11.16 ±0.39	10.24 ±0.59
	P value	<0.001**	<0.001**
Reticulocyte count	Before	0.72± 0.15	0.73 ±0.11
	After 4 wks	1.18 ±0.14	1.2 ±0.19
	P Value	<0.001**	<0.001**
Ferritin	Before	10.87± 2.3	12.5 ±3.1
	After 4 wks	83.54± 12.1	44.1± 6.3
	P Value	<0.001	<0.001

The parameters are compared before giving the drug, 4 weeks after giving the drug & during delivery.

1. Heamoglobin-

In Group A - The baseline mean Hb% was 8.13±0.35 gm%. After 4 wks of receiving the drug the Hb% mean was 10.33±0.34 & at delivery mean Hb% was 11.16±0.39 gm%. An mean Hb% increase by 2.2±0.44 gm% was seen at 4 weeks & 3.04± 0.5 gm% was seen at delivery. The P value is <0.001 which is statically significant.

Haemoglobin

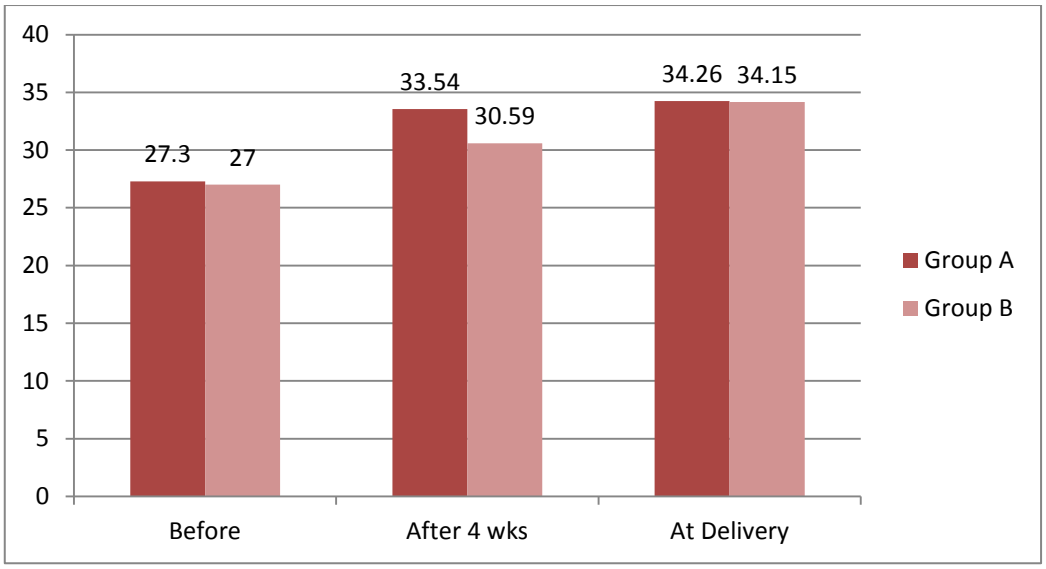


In Group B – The baseline mean Hb% was 8.052±0.22 gm%. After 4wks of receiving the drug the Hb% mean was 9.4±0.24 gm% & at delivery mean Hb% was 10.24±0.59. An mean Hb% increase by 0.8± 0.17 gm% was seen at 4 weeks & 1.72±0.5gm% was seen at delivery. The P value is <0.001 which is statistically significant.

2. Hematocrit –

In Group A – The Hematocrit before giving the drug was a mean of 27.33±2.5%. After 4wks of receiving the drug the mean was 33.54±1.6% & at delivery the mean was 34.2±2.3%. There was an mean increase by 6.22±2.2% at 4 wks & by 6.9±2.9% at delivery. The P value was statistically significant.

Hematocrit:

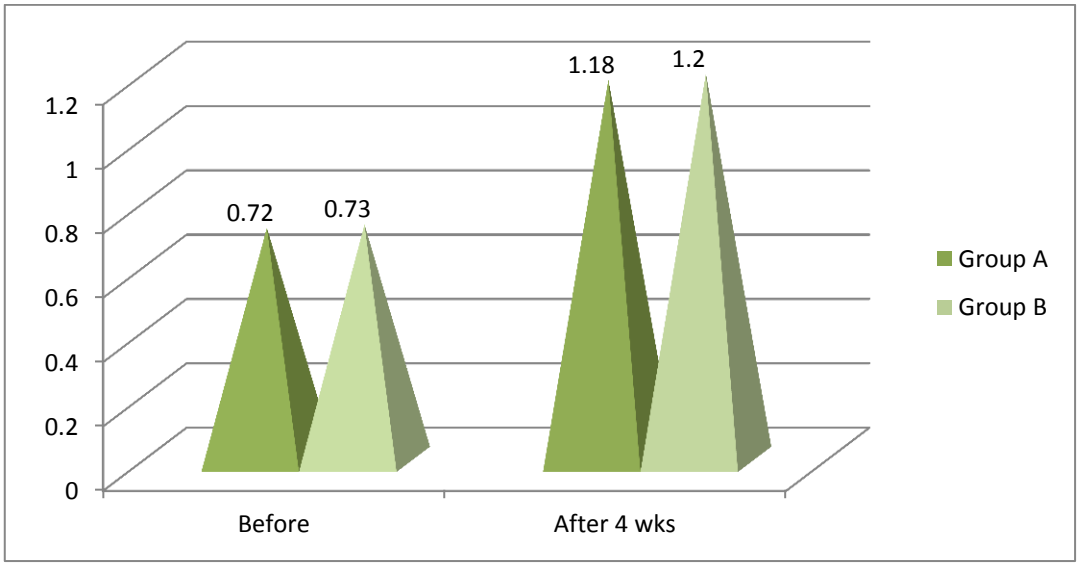


In Group B – The mean hematocrit before giving drug was 27.33±2.5%. After receiving the drug at 4 weeks mean was 30.5±1.3% & at delivery mean was 31.1±1.2%. There was an mean increase by 3.5±2.3% at 4 weeks & by 4.1±2.22% at delivery. The P value is statistically significant.

2. Reticulocyte count –

In Group A – The Reticulocyte count before giving drug was a mean of 0.72±0.1%. After receiving the drug was 1.18±0.14%. The increase in this Group was statistically significant.

Reticulocyte count:



In Group B – The Reticulocyte count before giving the drug was a mean of 0.73±0.11%. After receiving the drug was 1.2±0.19%. The increase in this Group was statistically significant.

3. Ferritin level –

In Group A –The mean ferritin level before giving the drug was 10.87±2.3ug/1. After receiving the drug at 4 weeks the mean was 83.54±12.13ug/1. There was a mean increase by 72.6±10.5ug/1 at 4 weeks. The P value is statistically significant.

In Group B – The mean ferritin level before giving the drug was 12.5±3.1%. After receiving the drug at 4 weeks mean was 44.13±6.3ug/1. There was a mean increase by 31.6±5.2ug/1 at 4 weeks. The P value is statistically significant.

FERRITIN

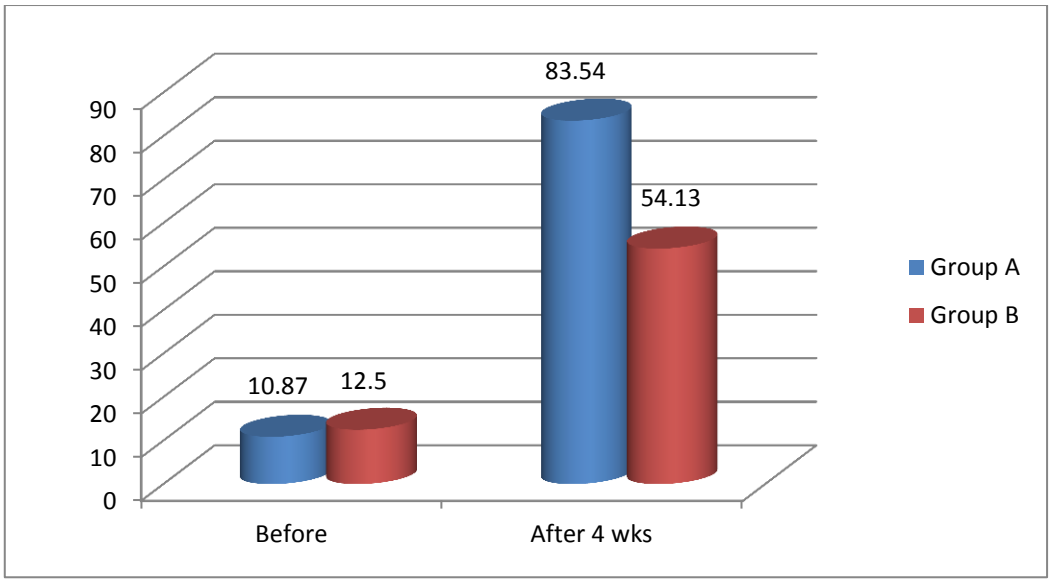


Table 3: Number and percentage of patients discontinued the treatment due to side effects

	Group A		Group B	
Drug	**(n=30)**		**(n=30)**	
	No	**%**	**No**	**%**
Received	**30**	**100.0**	**26**	**86.66**
Did not received	**0**	**0.0**	**4**	**13.33**

This table shows the number of cases who dropped out of the study due to side effects. In Group A all of them received iron, i.e. none of them developed such serious adverse effect to stop the infusion. In Group B 86.66% of the cases studied received the injections & other 13.33% due to severe adverse effects dropped out of the study.

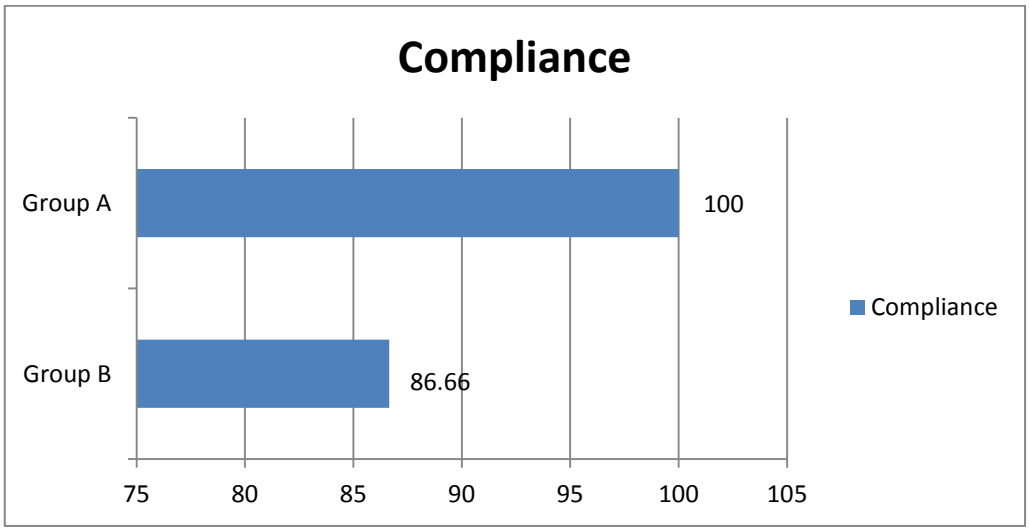
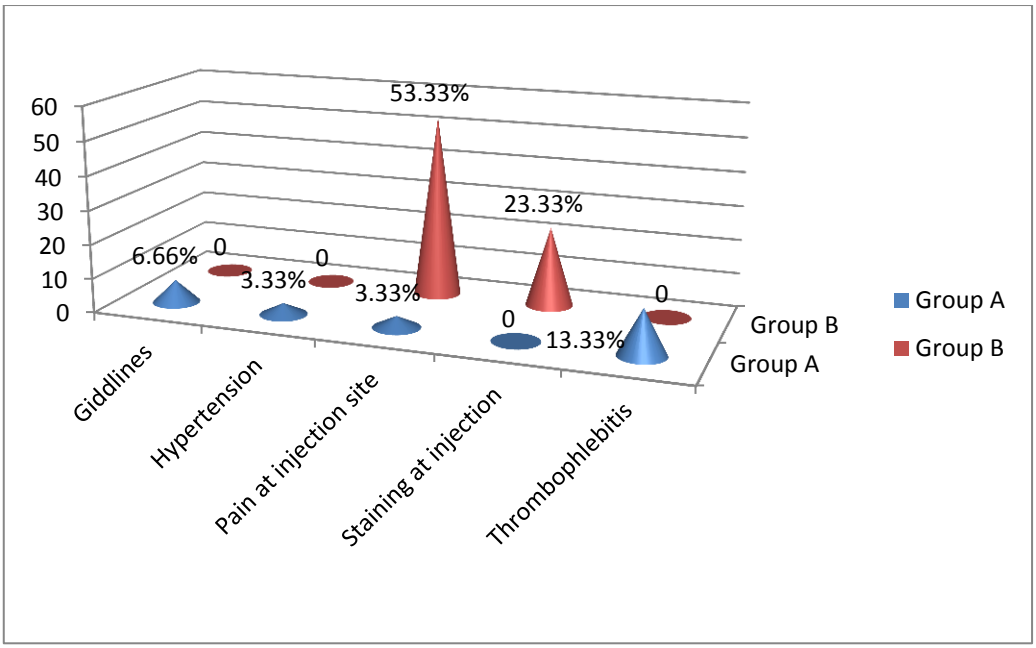


Table 4: Profile of Side Effects in Both the Groups

	Group A		Group B	
Side effects	**(n=30)**		**(n=30)**	
	No	%	No	%
1. Giddiness	2	6.66	0	0
2. Hypertension	1	3.33	0	0
3. Pain at injection site	1	3.33	16	53.33
4. Staining of the skin	0	0	7	23.33
5. Thromboplebitis	4	13.33	0	0

SIDE EFFECTS:



This table shows the profile of side effects in both the groups. In Group A 4 cases had Thrombophlebitis, I had transient raise in Blood Pressure after bolus injections, 2 had giddiness & I had pain at the injection site.

In Group B 16 cases had severe pain at the injection site & 6 had staining at the injection site. 4 cases in Group B dropped out of the study due to side effects.

4. DISCUSSION

Worldwide, iron deficiency is the most common cause of anaemia in pregnancy. More than half a million maternal deaths occur each year, approximately 90% of which are in developing countries, making evident a large discrepancy between developed and developing countries[3].

To ensure good Hemoglobin level at the time of delivery, parenteral iron will play a major role by ensuring definitive replenishment of iron stores.There are very limited studies of using Iron Sources during pregnancy & most of the studies are done of using iron sucrose in chronic renal failure patients.

In a Review article on Treatment of Iron Deficiency Anemia during Pregnancy, by Reveiz L, Gyte GML, Cuervo LG, published in *The Chochrane Library, 2007, Issue* 2, Author's conclusions were, Despite the high incidence and burden of disease associated with this condition, there is a paucity of good quality trials assessing clinical maternal and neonatal effects of iron administration in women with anaemia. Daily oral iron treatment improves haematological indices but causes frequent gastrointestinal adverse effects. Parenteral (intramuscular and intravenous) iron enhances haematological response, compared with oral iron, but there are concerns about possible important adverse effects. Large, good quality trials, assessing clinical outcomes (including adverse effects) are required.

In study conducted by A. Wali et al 40 cases were included in IV group & 20 in IM group[4]. In study by Zahid Hashmi et al 80 antenatal cases were selected who are 12-36 wks of gestation with anaemia. In present study 47% of them were in 28-32 wks of gestation, 21% of them had postpartum anemia[5].

In study done by Shailesh kore (2007), most of the cases belong to Low socio economic status. In present study 53.33% of them belong to Lower Middle class. In a study conducted by Bhandal N (2006), the baseline Hb% was 7.5±0.8 gm% after 4 wks of iron sucrose infusion the mean increase in Hb% 4±05.gm%[8].In study conducted by A. Wali et.al. on 60 pregnant women for efficacy of parenteral Iron Sorbitol, mean pre-infusion haemoglobin level was 8.8± 0.9 gm/dl and the mean increase in Hb% of 09.± 0.3gm%.

In a study conducted by Abdul-Kareem (2006), the baseline ferritin was 11.9±5.0 ug/1, after 4 wks of iron sucrose infusion the mean increase in ferritin was to 95.5±38. 1ug/1.In study conducted by Khurshid Shabbir et. al. The mean

baseline ferritin level was 9.6±3ug/1 and the mean increase in ferritin level was to 82±32.4ug/1[6]. In study done by Bhandal N (2006), there were no serious adverse effects reported, but 23% of them complained of metallic taste during infusion, 18% of them had facial flushing and pain at the injection site. In present study 18% of them showed mild side effects, 4 of them had thromboplebitis, 2 of them had transient hypertension after the infusion & 1 had rashers. In study done by A. Wali et al they used IM Iron Sorbitol with that 48% of them had side effects like, pain at the injection site and staining at injection site. In present study as in cases of Iron Sorbitol 13.33% of the cases had severe reactions amounting to stop the injection & 60% had mild to moderate reactions continuing the injections.

5. CONCLUSION

Even though Iron Sorbtol is as efficacious as Iron sucrose in raising the Hb level, the occurrence of more number of reactions restricts its use for intramuscular use. Iron Sucrose can be used as Observed Therapy ensuring definitive iron replenishment.

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