*IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)*
*e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 17, Issue 5 Ver. 13(May. 2018), PP 11-15*
*www.iosrjournals.org*

# Heme iron polypeptide Vs Iron sucrose for treatment of iron deficiency anaemia during pregnancy

*Sarika Singh[1], Sachin Kumar Singh [2]
[1] *Department of Obstetrics and Gynaecology, Central hospital, Dakra and Area Hospital, Bachra , Ranchi, Jharkhand,India*
[2]*Department of Surgery, RIMS, Ranchi, Jharkhand, India*
*Corresponding author: [*]SarikaSingh*

***Abstract***
***Background and objectives:****Anaemiais a global problem. Its prevalence in India is about 60% [1] and may increase to 80% during pregnancy [2] . Its directly or indirectly contributes to about 40% maternal death. Over 90% of anaemia is due to iron deficiency. WHO defines anaemia in pregnancy as Hb<11g/dl. Mild (Hb 10-10.9g/dl) and moderate (7-10g/dl) Iron deficiency Anaemia during pregnancy can be corrected by iron therapy either by oral or parenteral route This study is done to compare the oral heme iron polypeptide to intravenous iron sucrose therapy.*
***Methods:****This is a randomized comparative multicentre study done at Central hospital, Dakra and Area hospital, Bachra , Ranchi, Jharkhand, during the period august 2016 to June 2017 . Study population composed of pregnant mothers of 24 – 30wks who were admitted with anaemia. Inclusion Criteria- pregnant mothers>18yrs, gestational age 24wks-30wks ,Hb 7g/dl-10g/dl( only due to iron deficiency). 200 pregnant women of gestational age 24-30wks with Hb<10g/dl were included in the study and were randomly distributed to receive intravenous iron sucrose therapy and oral heme iron polypeptide therapy for period of three months. Out of 100 in oral iron therapy 11 were excluded on the basis of exclusion criteria, 5 did not come for follow up in antenatal visit and 6 could not tolerate oral iron therapy so only 78 women was left for study in oral iron therapy. And out of 100 in intravenous iron therapy 6 were excluded on basis of exclusion criteria ,3 went into preterm labour and 9 did not complete the therapy so only 82 women was left for study in intravenous iron therapy group.*
***Results:****After 3 months of treatment post treatment Hb level , serum ferritin , MCV and MCH level was observed in both the groups and it was found that there is no significant difference in the post treatment increase in the above factors between the two study group [ P>0.05] .*
***Conclusion:****Heme iron polypeptide is a safe and well tolerated oral iron preparation and HIP increases Hb level and serum ferritin level almost same as that of intravenous iron sucrose when used for treatment of iron deficiency anaemia in pregnancy. And HIP can be used safely in place of intravenous iron in mild and moderate anaemia in pregnancy.*
***Keywords:****HIP,iron sucrose, anaemia and pregnancy.*

---

Date of Submission: 09-05-2018 Date of acceptance: 26-05-2018

---

## I. Introduction

Anaemiais a global problem. Its prevalence in India is about 60% [1] and may increase to 80% during pregnancy [2] . Its directly or indirectly contributes to about 40% maternal death. During pregnancy there is increase in plasma volume(50%) and cell mass(18-25%) . This physiological changes causes dilutional decrease in haemoglobin concentration known as "physiological anaemia in pregnancy" and this is maximal at 32wks. Poverty , ignorance , malnutrition , food taboos , repeated pregnancy in limited period, parasitic and helminthic infestation and malaria contribute significantly and haemoglobinopathies to a smaller proportion of causation of anaemia in our country. Over 90% of anaemia is due to iron deficiency [3,4] , folate deficiency is a minor cause and vitamin B12 hardly causes anaemia. Cause of iron deficiency anaemia during pregnancy is increased requirements during pregnancy, infection during antenatal and postnatal period , blood loss during delivery. And rapid succession of pregnancy [5].

WHO defines anaemia in pregnancy as Hb<11g/dl and haematocrit <0.33. The Indian council of medical research categorizes anaemia as mild (10-10.9g/dl), moderate (7-10g/dl) , severe (<7g/dl) and very severe (<4g/dl). Maternal anaemia is an important cause of adverse outcome in obstetrics , perinatal and neonatal morbidity, blood transfusion and maternal mortality. Mild and moderate Iron deficiency Anaemia during pregnancy can be corrected by iron therapy either by oral or parenteral route.

On an average approximately 1000mg of iron is required during pregnancy. Iron is also conserved by amenorrhoea during pregnancy. After deducting this conserved iron 500-600mg of iron is required in pregnancy(i.e. 4-6mg /day ). Oral iron is available in two forms heme and non heme iron. Heme iron is better absorbed than non heme iron.

This study is done to compare the oralheme iron polypeptide to intravenous iron sucrose therapy.

## II. Materials And Methods

This is a randomized comparativemulticentre study done at Central hospital, Dakra and Area hospital Bachra , Ranchi, Jharkand, during the period august 2016 to June 2017 . Study population composed of pregnant mothers of 24 – 30wks who were admitted with anaemia. **Inclusion Criteria**- pregnant mothers>18yrs, gestational age 24wks-30wks ,Hb 7g/dl-10g/dl( only due to iron deficiency). **Exclusion criteria**- cause other than iron deficiency and women with history of blood transfusion in current pregnancy. 200 pregnant women of gestational age 24-30wks with Hb<10g/dl were included in the study and were randomly distributed to receive intravenous iron sucrose therapy and oral heme iron polypeptide therapy for period of three months . Out of 100 in oral iron therapy 11 were excluded on the basis of exclusion criteria, and 11 did not come for follow up in antenatal visit so only 78 women was left for study in oral iron therapy. And out of 100 in intravenous iron therapy 6 were excluded on basis of exclusion criteria ,3 went into preterm labour and 9 did not complete the therapy so only 82 women was left for study in intravenous iron therapy group.

Diagnosis of iron deficiency anaemia was done on basis of Hb concentration, serum ferritin level , mean corpuscular volume(MCV) and mean corpuscular haemoglobin(MCH).

Heme iron polypeptide (HIP) is produced by hydrolyses of bovine iron and its mode of action is different than other iron preparation . It is absorbed by receptors heme carrier protein -1, and is given in dose of one tab twice daily irrespective of the meal for the period of three months.

For intravenous dose, iron dose is calculated by the following formula "total iron needinmg = 2.4*pre pregnancy weight in kg* (target Hbconcentration – actual Hb concentration)g/dl +500mg." Target Hb is12gm/dl, 2.4 is the correction factor and500mg is the average stored iron in an adult pregnant women [ 6 ]. The calculated dose is given in 6-8 session , in each session 200mg of diluted in200ml normal saline every alternate day. The two study group is enquired for any types of side effects or intolerance during each antenatal visit. Folic acid is routinely given two all the patients in both the study groups. Treatment in both the study group is was continued for 3 months and the treatment efficacy was examined by measuring Hb concentration, serum ferritin, MCV and MCHafter 3 months of treatment.

**Statistical analysis**

Statistical analysis done by SPSS version 29and student T test for quantitative data analysis.

## III. Results

200 pregnant women of gestational age 24-30wks with Hb<10g/dl were included in the study and were randomly distributed to receive intravenous iron sucrose therapy and oral heme iron polypeptide therapy for period of three months . Out of 100 in oral iron therapy 11 were excluded on the basis of exclusion criteria, 11did not come for follow up in antenatal visit so only 78 women was left for study in oral iron therapy. And out of 100 in intravenous iron therapy 6 were excluded on basis of exclusion criteria ,3 went into preterm labour and 9 did not complete the therapy so only 82 women was left for study in intravenous iron therapy group.

The two study groups were matched with no significant difference in mean age ( HIP group 24.62 ± 3.44 and IV iron group 25.06± 3.04) , mean weight ( weight HIP group 58.82 ± 5.55 and IV iron group 59.02±5.49),parity( HIP group 2.75±3.64 and IViron group2.73±3.5) and mean gestational age( HIP group 26.94±1.9 and IV iron group 27.33±1.88) . (TABLE -1)

| variables | HIP Group | IV IronGroup | P value |
|---|---|---|---|
| Age (years) | 24.62 ± 3.44 | 25.06 ± 3.04 | 0.39 |
| Weight(kg) | 58.82 ±5.55 | 59.02 ± 5.49 | 0.8 |
| parity | 2.75 ± 3.64 | 2.73 ± 3.5 | 0.9 |
| Gestational age(wks) | 26.94 ± 1.9 | 27.33 ± .88 | 0.19 |

After 3 months of treatment post treatment Hb level (HIP group 11.55 ± 0.65 and in IV group 11.70 ± 0.62 ), serum ferritin ( HIP group 122.59 ± 5.34 and in IV group 123.42± 5.18 ) , MCV ( HIP group 90.69 ± 6.61 and IV group 91.15 ± 5.62 ) and MCH ( HIP group 25.62 ± 3.33 and IV group 25.82 ± 2.63 ) level was

observed in both the groups and it was found that there is no significant difference in the post treatment increase in the above factors between the two study group [ P>0.05] (TABLE 2) .

| Variables | HIP group | IV iron group | P value |
|---|---|---|---|
| Pre-treatmentHb | 8.25 ± 0.97 | 8.2 ± 0.95 | 0.74 |
| Post-treatment Hb | 11.55± 0.65 | 11.7 ± 0.62 | 0.14 |
| Pre-treatment ferritin. | 16.34 ± 2.54 | 17.20 ± 2.19 | 0.07 |
| Post-treatment ferritin | 122.59± 5.34 | 123.42 ± 5.18 | 0.3 |
| Pre-treatment MCV | 67.33 ± 4.90 | 66.44 ± 7.23 | 0.4 |
| Post-treatment MCV | 90.69 ± 6.61 | 91.15 ± 5.62 | 0.6 |
| Pre-treatment MCH | 23.12 ± 3.39 | 22.82 ± 4.20 | 0.6 |
| Post-treatment MCH | 25.62 ± 3.33 | 25.82 ± 2.63 | 0.7 |

During the three months treatment with oral iron polypeptide no major side effects was observed among the patients only for few minor side effects like black stool and minor nausea in patients on oral HIP . Only 3 out of 78( 3.8%) complained of minor side effects which did not cause non-compliance among them and among patients on intravenous iron there was complain of metallic taste during the period of injection and mild pain at the injection site.

## IV. Discussion

Iron deficiencyis the most wide spread nutritional deficiency in the world and it accounts for 75% of all types of anaemia in pregnancy. It is due to the fact that diet in pregnancy is insufficient to supply iron requirement which is about 4.4mg/day . It has high prevalence in developing countries.

Although one of the main target of WHO is prevention and treatment of anaemia in pregnancy ,it is still under evaluated problem in developing countries. Anaemia in pregnant women is considered harmful for fetal growth and fetal outcome. Low birth weight and preterm deliveriesassociated with impaired growth and mental and motor development , is linked to anaemia in pregnancy [7,8,9]. Preterm delivery is strongly associated with anaemia in third trimester. Kumar et al and Monika et al have found such an association when mothers are severely anaemic Hb<7g/dl,[10-14]. Other maternal complication associated with iron deficiency anaemia are increased risk of cardiac failure and death, decreased lactation and post-partum depression and emotional instability [15].

Thus the early detection and treatment of iron deficiency anaemia can reduce the complication. The American college of obstetrics and gynecology recommend obtaining a haemoglobin and haematocrit at the first antenatal visit and at the beginning of the third trimester. Hb<11g/dl and HCT<33% diagnose anaemia. For diagnosis of iron deficiency anaemia ferritin level is the diagnostic of iron deficiency anaemia. The American college of obstetrics and gynecology recommend obtaining ferritin level haematocrit at the first antenatal visit and at the beginning of the third trimester. In pregnant women with anaemia iron deficiency anaemia is diagnosed if serum ferritin level <30ng/ml. And if a women is not anaemic iron deficiency is diagnosed if serum ferritin level<15ng/ml.

For diagnosis of iron deficiency anaemia a complete blood count shows reduced Hb, reduced mean cell volume (MCV) [ normal reference range is 80-100fl ], reduced mean cell haemoglobin (MCH) [ normal range 27 -33pg/cell ] and decreased mean cell Hb concentration. Thus patients peripheral blood smear shows microcytic hypochromic cells but However MCH and MCV can be reduced in other conditions and a normocytic normochromic cell does not rule out iron deficiency anaemia [16]. Therefore serum ferritin is considered gold standard .

In the above study parameters low Hb, MCV,MCH and low ferritin level are used to diagnose iron deficiency anaemia as well as to see the response of iron therapy after three months of treatment .

The correction of iron deficiency involves appropriate diet and iron supplementation. WHO recommends prenatal iron supplements in low ,middle income countries as well as in many high income countries [17,18]. Oral iron therapy is the preferred mode of treatment . Formulations may contain bivalent ferrous a or trivalent ferric forms of iron with consideration that ferrous preparation is more easily absorbed , less expensive and needs lower numbers of intake compared to the ferric forms [19,20].

In may 2007, Medical features inc, received approval from health Canada to market a new oral iron supplement termed heme iron polypeptide for the treatment of iron deficiency anaemia. HIP has been widely used in America for treatment of iron deficiency since 2001. HIP is produced by hydrolysis of bovine haemoglobin.HIP is absorbed through a receptor that is different from the absorption mechanism of other iron salt. Some potential advantages of HIP over oral iron salts include a proposed lack of dietary and drug interaction as well as a reduction in gastro intestinal adverse effects [21,22,23 ].

Parental therapy is used in case of moderate and severe iron deficiency anaemia. Most commonly used parental therapy is iron sucrose. Shafi et al. in a study comparing parental iron sucrose with oral ferrous

ascorbate , intravenous iron sucrose produces more rapid increase in Hb concentration and serum ferritin level than oral ferrous ascorbate [24]. Also Al RA et al found that changes in Hb level from baseline was significantly higher with parenteral iron than the oral iron[29].

The above study was done to compare the oral HIP and the intravenous iron sucrose therapy and The study shows that after 3 months of treatment post treatment Hb level , serum ferritin , MCV and MCH level observed in both the groups and it was found that there is no significant difference in the post treatment increase in the above factors between the two study group.

Nissenson et al performed a test between HIP and intravenous iron in patients with chronic kidney disease and it was proved that oral HIP successfully replaced intravenous iron therapy in majority of patients resulting in maintenance of Hb level and serum ferritin level [25].

Hallberg et al also demonstrated that absorption of oral HIP is 10 times greater than that of other conventional oral iron [27]. HIP increased the serum level of iron 23 times greater than other ferrous iron formulations.

Ghadder et al also proved that oral HIP raised the Hb , serum ferritin , MCV and MCH value as significantly as intravenous iron after 3 months in patients with chronic kidney disease and all patients on intravenous iron can be shifted to oral HIP therapy with equivalent result to that of intravenous iron.

In additionBayoumeu et al Hb increase in intravenous group and in oral HIP after 30 days of treatment was without any significant difference.Hb increased from $9.6 \pm 0.79$ to $11.11 \pm 1.3$g/dl in intravenous group and from $9.7 \pm 0.5$ to $11.1 \pm 0.25$g/dl in oral iron group [26].Mishra et al also concluded that parenteral iron in iron deficiency anaemia is only needed when oral iron is ineffective due to malabsorption or noncompliance [ 28].

Thus my study shows that the efficacy of oral HIP is same as intravenous iron sucrose and patients on intravenous iron can be safely switched over to oral HIP with almost the same rise in Hb and serum ferritin level. However since there are limited data and studies about oral HIP, more studies are needed to compare the efficacy of the oral HIP to other oral and parental iron therapy.

HIP is a safe oral iron and have only minor side effects compared to the other oral ferrous preparations. Common side effects are nausea , acidity, upset stomach , diarrhoea and constipation. Pena – Rosas et al have shown that pregnant women receiving oral iron are more likely to develop gastrointestinal side effects particularly at dose $\geq$ 60mg elemental per day [30]. Pregnant women receiving intermittent oral iron had less side effects than those receiving daily dosing [31]. Thus iron given in <50mg/day have lesser side effects and is better tolerated by the patients [32].HIP have fewer side effects and higher absorption than other oral ferrous formulations because HIP is absorbed through a receptor that is different from the absorption mechanism of other iron salt.

In the above study only 3 out of 78 (3.8%) patients on oral HIP complained of minor gastro intestinal upset which did not cause noncompliance . AI Momen et al in his study showed that 30% of the patients on oral ferrous sulphate had poor compliance [33].

## V. Conclusion.

Heme iron polypeptide is a safe and well tolerated oral iron preparation and HIP increases Hb level and serum ferritin level almost same as that of intravenous iron sucrose when used for treatment of iron deficiency anaemia in pregnancy. And HIP can be used safely in place of intravenous iron for treatment of mild and moderate anaemia in pregnancy.

**Acknowledgment**
I am grateful to all the women who agreed to participate in the study .

**Disclosure**
Authors declare no conflict of interest.

## References

[1]. Schwartz WJ, Thurnau GR. Iron deficiency anaemia in pregnancy. Clinobstet and gynecol1995;38:443-54.
[2]. World health organisation. WHO global database. Geneva ,WHO,1997.
[3]. Bhatt R . maternal mortality in india- FOGSI-WHO study. J obstetgynecolind 1997;47:207-14.
[4]. Viteri FE . the consequences of iron deficiency and anaemia in pregnancy. Advexp med boil 1994;352:127-39.
[5]. Prema K, Neela KS, Ramalakshmi BA. Anaemia and adverse obstetric outcome. Nutr rep int 1981;23:637-43.
[6]. Barut A,Harma M. Intravenous iron treatment for iron deficiency anaemia idn pregnancy. J Turkish germangynecol association.2009;10:109-15.
[7]. Xiong. X Buekens , P Alexander , S Demianczuk, N Wollast, E. Anaemia during pregnancy and birth outcome. A metaanalysis.Am. j. Perinatol.17,137-146(2000).
[8]. Allen ,LH. Anaemia and iron deficiency: effects on pregnancy outcome. Am .j. clin .nutr.71(suppl.5) , 1280S-1284S(2000).
[9]. Rasmussen, S,Oian, P. First and second trimester Hb level and relation to birth weight and gestational age. Acta Obstet. Gynecol . scand. 72,246-251 (1993).
[10]. Rusia , U, Madan, N, Agarwal, N,Sikka,M,Sood,SK. Effect of maternal anaemia in fetal outcome. Indian j. Pathol.microbiol. 38,273-279 (1995).

[11]. Maternal anaemia in pregnancy is an independent risk factors for low birth weight and preterm delivery. Eur .j.obstet. gyneolreprod. Biol .122, 182-186(2005)
[12]. karasahin E, ceyhan ST, Goktolga U, Baser I. Maternal anaemia and perinatal outcome. Perinatal journal.15(30),127-130(2007).
[13]. Maternal and perinatal outcome in varying degrees of anaemia. Int .j. gynaecol . obstet .79,93-100(2002). Malhotra ,sharmaabatraamurthy, aroraa.
[14]. Kumar KJ, Asha N, Murthy DS , Sujatha M, ManjunathV.maternal anaemia in various trimesters and its effect on new born weight and maturity: an observational study. Int .j. prev med. 4(2),193-199 (2013).
[15]. Milman M. Iron prophylaxis in pregnancy- general or individual and in which dose?. Ann .hematol .7(11),599-610(2010).
[16]. Bermejo and gracia - lopez (2009)
[17]. CDC . recommendations to prevent and control iron deficiency in US. MMWR recommend. Rep ,47(RR-3):1-36.
[18]. International nutritional anaemia consultative group, WHO ,UNICEF guidelines for the use of iron supplements to prevent and treat iron deficiency anaemia. Stoltzfus RJ , Dreyfuss ML(eds) ILSI press, Washington DC, USA(1998).
[19]. Santiago P, ferrous versus ferric oral iron formulations for the treatment of iron deficiency anaemia: a clinical overview. Scientific world journal 2012, 846824(2012).
[20]. Berber I, DiriH, Erkurt MA, Aydogdu I, Kaya E, Kuku E. Evaluation of ferric and ferrous iron therapies in women with iron deficiency anaemia . adv . hematol 2014 , 297057(2014).
[21]. Grasbeck R, Kouvonen I, Lundberg M, Tenhunen R. An intestinal receptor foe heme . scand j haematol.1979;23:5-9.
[22]. UzelC,Conrad ME. Absorption of heme iron. Semin hematol.1998;35:27-34.
[23]. Seligman PA, Moore GM, Schleicher RB. Clinical studies of HIP: an oral heme iron product. Nutr res 2000;20:1279-86.doi:10.1016/S0271-5317(00)00215-3.
[24]. ShafiD, Purendre SV, Sathe AV. Iron deficiency anaemia in pregnancy: intravenous versus oral route. J. Obstet. Gynecol .india.62(3),317-321(2012).
[25]. Nissenson AR, Berns JS, Sakiewicz P, GhaddarS, Moore GM, Schleicher RB et al. Clinical evaluation of heme iron polypeptide sustaining a response to rHuEPO in hemodylasis patient . amj kidney disease 2003;42(2):325-330.
[26]. Bayoumen F , Subrian – Buisset C, Baka NE, et al . iron therapy in iron deficiency anaemia oral versus intravenous route. Am j . obstet. Gynecol. 2002;186(3):518-522.
[27]. Hallberg L, Hulten L, Gramatkovski E. Iron absorption from the whole diet in men :how effective is the regulation of iron absorption? Amjclinnutr. 1997;66:347-356.
[28]. MishraA , Dave N, Viradya K,. Fatal anaphylactic reaction with iron sucrose in pregnancy. Indain j pharmacol. 2013 ; 45(1):93-94.
[29]. AI RA, Unlubilgin E, Kandemir O . et al. Intravenous iron versus oral iron for treatment of anaemia in pregnancy. A randomized trial. obstetgynecol .2005.106:1335-40.
[30]. Pena –Rosas JP, De RegilLM,DowswellT,Viteri FE.(2012). Daily oral iron supplementation during pregnancy. Cochrane database syst rev12:cd004736.
[31]. Pena –Rosas JP, De RegilLM,DowswellT,Viteri FE.(2012).intermittent oral iron supplementation during pregnancy. Cochrane database syst rev12:cd004736.
[32]. Mc DiarmidT,Johnson ED (2002). Clinical enquiries . are any oral iron formulations better tolerated than ferrous sulphate? J fam pract 51:576.
[33]. Al MomenAK,alMeshari A al –Nuaim L et al.eur j obststgynecolbiol. 1996;69:121-4.

SarikaSingh "Heme iron polypeptide Vs Iron sucrose for treatment of iron deficiency anaemia during pregnancy. "IOSR Journal of Dental and Medical Sciences (IOSR-JDMS), vol. 17, no. 5, 2018, pp 11-15