Original Article

Effect of Venofer(Iron) Infusion Versus Oral Iron on Sonographically Monitored Perinatal Weight During Third Trimester in Pregnancy Anemia

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Abstract

Objective: To determine the effect of venofer iron infusion versus oral Iron on sonographically monitored perinatal weight during the third trimester of pregnancy among women with anemia.

Methodology: This descriptive case control study was conducted at the Department of Radiology in collaboration with the Department of Obstetrics and gynecology, Sir Syed Hospital, Karachi, from February 2019 to March 2020. Pregnant women with small for gestational age fetuses on ultrasound during 28–32 weeks of gestational age were recruited in the study. On ultrasound, the intrauterine fetal weight was estimated and the projected weight on birth was estimated following the growth-chart. The effect of iron therapy was measured by comparing fetal weight projected on ultrasound before iron therapy and the neonatal weight at birth.

Results: Pretreatment fetal weight on ultrasound was less than 2000 gm during 30–36 weeks of gestational age in both groups. An ultrasound projected weight at birth after treatment was estimated, the mean perinatal weight was 2481.94±292.91 grams in IV iron group and 2320.0±180.97 grams in the oral iron group, which was statistically non-significant (p=0.059). But neonatal birth weight was significantly higher in the IV iron group than in the oral iron group i.e. 2595.56±258.73 vs. 2394.71±202.09 (p=0.016).

Conclusion: Thus, it is concluded that venofer IV iron therapy for treating severe anemia is significantly effective in improving hemoglobin level and to achieving a normal birth weight compared to ultrasound predictive birth weight before and after IV treatment.

Keywords: Anemia, iron infusion, birth weight, ultrasound, third trimester

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Introduction

Iron is an essential element in that plays a significant role in many cellular function and processes, growth and development particularly in females of reproductive age. The most common dietary deficiency in the world is iron deficiency.[1] Iron deficiency anaemia is responsible for nearly half of all anaemia occurrences worldwide; due to the increased iron requirement during pregnancy, it may cause maternal anaemia and reduced baby iron reserves.[2] Because of iron deficiency, the concentration of hemoglobin also reduced and results in anemia. Typically, less than 7 g/dL hemoglobin level during pregnancy is considered severe anemia that required medical treatment. In developed nations, this condition affects 18% of people, while it affects 35–75 percent of people in developing countries[3] including in Pakistan 29% to 50%[4] and rate of anemia likely to increase by 66.7% in 2nd and 3rd trimester due to rapid fetal growth[5], as a

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result maternal biochemical markers particularly iron and hematocrit level fluctuate. The increased demand must be met by increased increasing maternal iron consumption from 6 mg per day in 1st trimester to 19 mg per day in 2nd trimester and 22 mg per day in 3rd trimester.[6] Since, hemoglobin plays a key role in transportation of oxygen from the lungs to different tissues of the body, resulting in reduced oxygen supply to the fetus and leads to adverse pregnancy outcomes for example low birth weight, pre-mature delivery or intrauterine growth retardation, stillbirth, increased susceptibility to infections or premature rupture of membranes.[7-9] Earlier, it was believed that even if maternal iron status is poor, fetal Hb production will not suffer, but now this is an outdated theory. Maternal anemia may result in fetal anemia and many other perinatal adverse effects.[10-11] Multi - nutrient supplements are prescribed throughout the pregnancy time period to cover deficiencies but in some of the cases when speedy correction is considered necessary or GI malabsorption or any active disease lowers iron absorption, then parental iron is the alternate treatment.[12-14] There may be three options for intravenous iron therapy i.e. low-molecular weight iron dextran, sodium ferric gluconate and iron sucrose.[14]

Iron Sucrose is best tolerated due to its lesser side effects[15] therefore present study was conducted over Venofer for treating Iron deficiency anemia. Iron Sucrose is promptly transported to the bone marrow for erythropoiesis and to the liver and spleen's reticuloendothelial system for iron storage.[16] The major advantage of Iron Sucrose is whether, unlike iron dextrans, it does not require a test dose when used for the first time.[17] The dose of intravenous iron sucrose was carefully administered for the first 20 minutes to check for any adverse reactions, then the complete amount was infused.[18] Fetal surveillance during the antenatal period before and after iron therapy among anemic mothers and fetal growth is very important for a desirable fetal outcome. For fetuses delivered between 22 and 34 weeks of gestation, Hadlock estimated fetal weight formula was even more appropriate than intergrowth formula.[19] There were multiple trials and studies done to measure the effect of iron therapy on maternal iron levels and fetal outcomes however, this study had novel feature related to effect of iron therapy on intrauterine fetal weight estimation and forecast for a reasonable birth weight in order to improve maternal iron level, its impact on fetal growth and fetal surveillance for guidance of maternal and child health practitioners to make appropriate action plans for healthy feto-maternal outcomes.

Methodology

This descriptive case control study was conducted in Sir Syed Hospital, Karachi, Pakistan over a period of 1 year from February, 15, 2019 to March 31, 2020. After taking informed consent, the sinologist & consultant radiologists were unaware about the gestational age by dates and by early ultrasound before performing estimated fetal weight (EFW). Pregnant women with hemoglobin level <8.0 gm/ dl and had small for gestational age fetuses on ultrasound during 28-32 weeks of gestational age were recruited in the study. The women having antenatal abnormal bleeding, polycystic ovary, thalassemia, liver abnormality on LFT and women with any malignancy were excluded from the study. The woman having Hb level 7-8 gm/ dl were randomly assigned by employing slip envelop draw method either intravenous or oral iron therapy group. However, the women with Hb<7 to 8 gm/ dl were deliberately given IV iron therapy.200 mg of Venofer was diluted in 200 mL of normal saline and given as an intravenous infusion for 1 week on alternate days.

The first 10–15 mL of iron sucrose was administered over 15 minutes (50 mL/hr) when it was given during the first time. If no adverse reactions were observed, the rate of administration was gradually increased to 100 mL/hr, or about 14 mg/min, with a maximum of 20 mg/min. In the event of an allergic reaction, proper precautions were taken. Ferrous sulfate oral iron treatment for 2 weeks was given 325 mg (65 mg of elemental iron) orally three times a day, lower doses first 2 days 35 mg of elemental iron daily may be as effective and cause fewer side effects. In next 12 days, 65 mg of elemental iron in addition to vitamin C (500 units) for absorption of iron. The women were asked to return the empty blister packs and describe the color of their stools in order to assess their medication compliance. In the both study groups, all major and minor side effects were documented. Hb test after treatment was repeated to compare the effect of iron therapy on hemoglobin concentration in both groups. Using ultrasound machine Toshiba Nemico XG, intrauterine estimated fetal weight (EFW). EFW was taken at time of antenatal visit during 28-36 weeks and after treatment of pregnancy anemia before delivery and a projected weight on birth was estimated. Low birth weight (LBW) is characterized as a first weight of less than 2500 g documented during hours of birth. According to WHO guidelines, VLBW (very low birth weight) is 1500 g, whereas ELBW (extremely low birth weight) is 1000

g.[20] The effect of iron therapy was measured by comparing fetal weight projected on ultrasound before iron therapy and neonatal weight at birth. All the relevant information including women's age, parity & booking statuses, comorbid, hemoglobin levels before and after treatment, perinatal weight before and after delivery were documented on proforma. SPSS-26, was used for statistical analysis.

Results

Mean age of the pregnant women was30.8±4.62 years and the average parity was 2.0±1.0 weeks. Most of the women in both groups were booked (p=0.898). Both groups were similar with respect to age distribution, booking and parity statuses. Of 35 women, 4 (11.4%) had gestational diabetes and 3 (8.6%) had hypertension. The proportions of gestational diabetes and hypertension were although higher in IV iron group, however statistically non-significant. (Table I)

Iron deficiency due to pregnancy anemia based on hemoglobin level was significantly higher in IV iron group as compared to oral iron group before iron therapy (p=0.008). A dramatic improvement in hemoglobin levels in IV iron group was seen after treatment as mean Hb was 9.183±0.549 gm/ dl as compared to oral iron group 8.641±0.507 (p=0.005) as detailed in table II.

Table I: Demographic characteristics and past medical history (n=35)

Variables	IV iron (Venofer) n = 18	Oral iron(Control) n = 17	P-value
Age			
25 or below	9 (50)	9 (52.9)	0.862
> 25	9 (50)	8 (47.1)	
Booking status			
Booked	17(94.4)	15 (88.2)	0.512
Un-booked	1 (5.6)	2 (11.8)	
Parity status			
Primiparous	7 (38.9)	6 (35.3)	0.455
2 – 3	8 (44.4)	10 (58.8)	
>3	3 (16.7)	1 (5.9)	
Comorbid			
Gestational diabetes	3 (16.7)	1 (5.9)	0.237
Hypertension	2 (11.1)	1 (5.9)	0.581

Pretreatment fetal weight on ultrasound in both groups was statistically similar (p=0.808), which was below than 2000 gm during 30-36 weeks of gestational age. An ultrasound projected weight at birth after treatment was estimated, the mean perinatal weight was 2481.94±292.91 grams in IV iron group and 2320.0±180.97 grams in oral iron group which was statistically non-significant (p=0.059). But neonatal birth weight was significantly higher in IV iron group than oral iron group i.e. 2595.56±258.73 vs. 2394.71±202.09 (p=0.016) as detailed in table II.

Table II: Effect of iron therapy on maternal hemoglobin levels and perinatal weight (n=35)

Variables	IV iron (Venofer) n = 18	Oral iron(Control) n = 17	P-value
Hemoglobin levels before treatment	6.928±0.344	7.276±0.390*	0.008
Hemoglobin levels after treatment	9.183±0.549*	8.641±0.507	0.005
Pretreatment fetal weight on ultrasound	1964.72±215.07	1979.71±135.96	0.808
Gestational age at perinatal birth	40.61±1.614	40.94±1.144	0.492
Post-treatment ultrasound projected weight at birth	2481.94±292.91	2320.0±180.97	0.059
Perinatal birth weight	2595.56±258.73*	2394.71±202.09	0.016

Discussion

Pretreatment fetal weight on ultrasound in both groups was statistically similar (p=0.808), which was less than 2000gm during 30-36 weeks of gestational age. An ultrasound projected weight at birth after treatment was estimated, the mean perinatal weight was 2481.94±292.91 grams in IV iron group and 2320.0±180.97 grams in the oral iron group which was statistically non-significant (p=0.059). But neonatal birth weight was significantly higher in IV iron group than oral iron group i.e. 2595.56±258.73 vs. 2394.71±202.09 (p=0.016). Our study results were comparable with a similar study done by Gupta A et al who reported the same outcome parameters comparing IV versus oral iron groups. However, they reported non-significant difference of neonatal birth weight in both the groups, being 2607 ± 253.28gm in the I/V group &2568 ± 244.19 gm in the oral group.[16] Our study has addressed a good fetal surveillance during antenatal period in anemic pregnant women who were treated for Hb improvement in addition to preventing low neonatal birth weight, need of blood transfusion in case of cesarean section delivery. In an Indonesian study, the effect of anaemia on neonatal birth weight was studied, and it was discovered that neonates

of anaemic mothers weighing more than 2,500 g at birth had a nearly 2-fold increased risk of low hemoglobin (100 g/L) at 3–5 months comparison to the non-birth weight newborns of non-anemic mothers; those weighing less than 2500 g were at an increased risk of anaemia. Low-birth-weight infants born to moms who did not have anaemia, on the other hand, were not at an increased risk.[21] Our study has greater strength over this study that we treated anemic patients and measured weight before and after delivery. There are various potentially adjustable hurdles to IV iron use that may need to be addressed in order for IV iron to be offered to obstetric patients who cannot tolerate oral formulations or who require quick iron replenishment[22], a reduced fetal growth in mid-pregnancy.[23] On other hand, some authors have shown the effectiveness of supplementation (30 mg/day) that it significantly increases birth weight and lower the incidence of preterm delivery. However, after controlling for confounding factors, foetal biometry and growth were not affected by the consumption of dietary iron however, after controlling for confounding factors such as dietary iron consumption, the infants of mothers who took iron supplements had biparietal diameter and belly circumference that were 0.09 cm (P = 0.012) and 0.39 cm (P = 0.017) larger than the newborns of mothers who did not take iron supplements.[26] Another study comparing the outcomes of newborn babies, There was a 6.5% increase in low-birth-weight newborns and a 11.5 percent increase in preterm deliveries in mothers who were anaemic in their third trimester of pregnancy.[5] Expertise of radiologist sonographer is very important during the antenatal weight measurement in third trimester. In a study measuring accuracy of ultrasonographic fetal weight measurement, has shown serious reservations about estimated fetal weight (EFW) and reported that correct (deviation from birth weight ≤ 10%) EFW was seen in 72.2% of cases with the fetal biometry; 19.7% were underestimated, and 8.1% were overestimated.[27]

Conclusion

Thus, it is concluded that venofer IV iron therapy for the treatment of severe anaemia is significantly more effective than ultrasound predictive birth weight before and after IV treatment in improving haemoglobin levels as well as foetal growth to achieve a normal birth weight. It also reduces the chance of blood transfusion in case of operative delivery.

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