Low-Dose Weekly Intravenous Iron Sucrose versus Daily Oral Iron for Iron Deficiency Anemia in Late Pregnancy: A Randomized Controlled Trial

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Objective: To compare the efficacy of low-dose weekly intravenous iron sucrose with oral iron for iron deficiency anemia (IDA) in late pregnancy.

Material and Method: Eighty singleton pregnant women with IDA at 33 weeks gestation were randomized to receive either oral ferrous fumarate 200 mg of elemental iron daily until delivery (OFF-group) or 200 mg of intravenous iron sucrose complex weekly up to 500 mg (ISC-group). Hematological and complete iron profiles were assessed at 36 weeks gestation and at delivery. Pregnancy outcome and adverse drug reaction were recorded.

Results: A gradual increase of hemoglobin (Hb) level was observed in both groups at 36 weeks' gestation and at delivery. Median serum ferritin level in the ISC-group was 4.7 times of that in the OFF-group at 36 weeks' gestation (123.8 (90.4, 176.2) vs. 26.2 (18.9, 38.1) μ g/L; p<0.001) and remained 2.3 times at delivery (66.3 (32.6, 93.7) vs. 28.3 (20.6, 38.9) μ g/L; p<0.001). No serious side effect was detected. Both groups had similar mean infant birth weight.

Conclusion: Low-dose intravenous iron sucrose complex in weekly divided infusions is more efficacious in replenishing iron storage but not more efficacious in raising hemoglobin level compared with daily oral ferrous fumarate for pregnant women with IDA in late pregnancy.

Keywords: intravenous iron sucrose, oral iron, iron deficiency anemia, hemoglobin, serum ferritin, iron storage

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Anemia in pregnancy is a significant worldwide problem with an average prevalence of 42% ranging from 5.7% in some states of USA, 25% in the UK, to 75% in Gambia^(1,2). A major cause of anemia in pregnancy is iron deficiency. As iron requirement increases remarkably during pregnancy, it cannot be met by dietary intake alone. Despite the general prescription of oral iron during antenatal care, anemia in the third trimester is still prevalent and was reported to be 37.8% in Thailand^(1,3). This is often due to poor compliance mainly from patient's intolerability to oral iron side effects or forgetfulness. Moreover, certain food or drinks⁽⁴⁾ and some gastrointestinal (GI)

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third trimester, only a short period of time is available to rectify iron deficiency anemia (IDA) before delivery. Intravenous (IV) iron can be an alternative to circumvent the problems related with oral iron therapy. Unlike parenteral iron used in the past which was associated with high rates of anaphylactic reaction, current IV iron formulations have been used with much more acceptable safety⁽⁵⁻⁹⁾. Among various types of IV iron complexes, iron sucrose complex (ISC) has been reported to be associated with a very low rate of adverse events at 5.25 per million units sold⁽⁶⁾. The recommended total dose of ISC for

conditions hamper iron absorption. When found in the

a pregnant woman is calculated using Ganzoni formula as follows: prepregnancy weight (kg) x (target Hb-actual Hb) (g/L) x $0.24+500 \text{ mg}^{(10)}$. Roughly, the average amount of ISC to be given is about 800-1,000 mg. It should be administered at the maximum amount of 200 mg per infusion per day and

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has been recommended to be given every 2-3 days to meet the required dose. Thus, it causes significant physical and financial burden to patients for their hospital revisiting to complete the treatment protocol. Interestingly, a lower dose of ISC (700 mg by average) can effectively raise mean Hb level of pregnant women from 8.5 to 12.0 g/dL within 14 days(11). Nevertheless, the efficacy in IDA treatment during pregnancy between ISC and oral iron tablets remains inconclusive. In some studies, hemoglobin (Hb) could be raised faster and higher in the ISC-group^(7,12) while one study showed no difference in Hb rising but showed the increased serum ferritin level in the ISC-group⁽⁵⁾. Serum ferritin, in the absence of inflammation, reflects body iron store and can be used to detect iron depletion or deficiency^(13,14). However, the minimal dose of IV iron to replenish iron storage is still unknown.

In the present study, the authors compared the efficacy of low dose ISC (500 mg) given in weekly divided doses with oral iron in replenishing the iron storage in the third trimester IDA pregnant women after 3-week treatment and at delivery. The iron status at 3 weeks after treatment (36 weeks gestation) was set as the main study objective as it is the time that labor and delivery could possibly take place. Hb and hematocrit (Hct) levels were also determined; additionally, patient compliance and drug safety were also recorded.

Material and Method

The trial was conducted at Maternal and Fetal Medicine Unit, Faculty of Medicine Siriraj Hospital, Mahidol University. The research protocol was reviewed and approved by the Siriraj Institutional Review Board (No. 296/2551 (EC3)). The trial was also registered with ClinicalTrial.gov (ID No. NCT 00746551).

Singleton pregnant women aged 18-45 years old with anemia (Hb level <11.0 g/dL or Hct <33.0 %) found at gestational age (GA) of 32 weeks were invited into the study. With patient's informed consent, 20 ml of blood was obtained to determining serum ferritin, serum iron (SI), total iron binding capacity (TIBC), Hb typing and C-reactive protein (CRP). Stool examination for parasitic infection was also performed.

Complete blood count to determine Hb level and Hct was performed by Coulter LH780 automated analyzer. Serum ferritin was determined using electrochemiluminescence immunoassay (ECLIA). A special iron-free tube was used for iron study. Iron concentration was determined by the intensity of a coloring agent which reacts with the iron released from transferrin. Hb typing was performed using high performance liquid chromatography. C-reactive protein was performed by particle enhanced immunoturbidimetry.

At GA of 33 weeks, patients who met the criteria of IDA consisting of ferritin level <15 μ g/L, CRP of <20 mg/L⁽¹⁵⁾ and whose stool examination revealed no parasites were recruited into the present trial. Patients were excluded if they had a history of allergic reaction to iron drug, anemia form other medical diseases such as thalassemia diseases, previous preterm birth and blood donation or transfusion within the past 120 days. Patients who did not follow the medication protocol, lost follow-up during the first 3 weeks or delivered at less than 3 weeks after the medication had been started were withdrawn from the study.

For sample size determination to compare the increase of serum ferritin level between patients receiving intravenous iron sucrose and oral ferrous at 3 weeks, the difference by $100\pm150 \text{ µg/L}$ or greater was used in the calculation formula⁽⁵⁾. By setting the probability of 2-sided type I error and the power of test at 0.05 and 80%, respectively, a minimum of 36 participants in each group had to be enrolled to the study.

The eligible population was randomized according to the number contained in the opaque envelope into 2 groups by the research nurse who was responsible for drug administration: the intravenous iron sucrose complex group (ISC-group) and the oral ferrous fumarate group (OFF-group). The number was already block randomized with size of 4 by nQuery Advisor[®] software (version 6.01; Statistical Solutions Ltd., Cork, Ireland, United Kingdom).

The patients in the OFF-group were instructed to take 3 oral ferrous fumarate tablets daily (a total of 200 mg elemental iron per day) from randomization until delivery. The remaining of OFF tablets was counted at every visit to evaluate compliance. Patients who consumed OFF less than 80% of the requirement were withdrawn from the trial.

In the ISC-group, patients were administered 500 mg of ISC (Venofer[®], Vifor International AG, St. Gallen, Switzerland) in three divided doses, i.e., 200 mg at 33 and 34 weeks' and 100 mg at 35 weeks' gestation. No other iron supplementation was further given to this group until delivery. In preparation, 200

mg of ISC was diluted into 100 ml of 0.9% NaCl solution. A test dose by a slow injection of 5 ml of solution within 5 minutes was performed in the first ISC infusion. If no adverse reaction was observed in 15 minutes, the remaining solution was infused to the patient within 30 minutes. The infusions in subsequent weeks were administered within 40 minutes. Post infusion observation was performed in every visit for at least 30 minutes to ensure patient safety.

Serum ferritin, Hb, Hct, SI and TIBC at GA of 36 weeks and at delivery were measured. To determine the weekly responses of these blood parameters, 3-consecutive-week blood samplings were also performed in the first 10 patients of each group. Patient compliance and side effects were also evaluated in every visit. Neonatal birth weight and gestational age at delivery were recorded.

Statistical analyses were performed using SPSS version 18.0 software (SPSS, Inc., Chicago, Illinois, USA). Maternal demographic data was presented in mean \pm standard deviation (SD) and percentage. Independent t-test, Mann-Whitney U test and Pearson Chi-Square test were used where appropriate for comparison between the 2 groups. A *p*-value of <0.05 was considered statistically significant.

Results

One hundred and ninety-four anemic patients were approached but 104 cases were excluded because their serum ferritin was >15 μ g/L and 10 cases refused to enter the trial. Finally, 80 eligible patients were randomized into 2 groups of OFF-group (n = 40) and ISC-group (n = 40). The majority of the women (67/80) were mildly anemic with Hb >9 g/dL.

At GA of 36 weeks which was the time of the study main objective, 4 cases of the OFF-group and 2 cases of the ISC-group did not have their blood taken. At delivery, 24 more patients (11 cases in OFF group and 13 cases in ISC group) were excluded from analysis due to loss of follow-up or preterm deliveries (Fig. 1). Patient demographic data in both groups were similar in terms of age, body weight and body mass index (BMI) (Table 1). All patients had a normal CRP level. Initial hematological parameters and iron status were also similar (Table 2). Median values of Hb and serum ferritin were 9.8 vs. 9.8 g/dL and 7.7 vs. $7.1 \mu g/L$ in the OFF-group and the ISC-group, respectively.

At 36 week's gestation, the improvement of blood parameters and iron status were shown by the increasing of Hb, Hct, serum ferritin and SI and the lower TIBC in both groups (Table 2). Table 3 showed the weekly trend of improvement during this 3-week period. The increasing trends of Hb and Hct lasted until delivery for both routes (Table 2 and Fig 2). Hb level in the ISC-group was slightly higher than the OFFgroup at GA of 36 weeks (10.7 vs 10.5 g/dL, p = 0.09) but was indifferent at delivery (11.5 vs 11.6 g/dL, p =0.76) (Table 2). Importantly, the improvement of serum ferritin was more obvious in the ISC-group right from the first week of treatment and continued rising to its peak in the third week (166.5 μ g/L) (Table 3 and Fig. 3). Serum ferritin in the OFF-group increased slowly up to delivery while that in the ISC-group declined after the third week, yet was still higher than that of the OFF-group at delivery and higher than the initial level (Table 2 and Fig. 3). In details, median serum ferritin level in the ISC-group was 4.7 times greater than that of the OFF-group at GA of 36 weeks [123.8 (90.4, 176.2) vs. 26.2 (18.9, 38.1) μ g/L; p<0.001] and remained 2.3 times at delivery [66.3 (32.6, 93.7) vs. 28.3 (20.6, 38.9) µg/L; p < 0.001 (Table 2 and Fig. 3). There was no difference in improvement of Hct, MCV, SI and TIBC between the two groups (Table 2.). Serum ferritin, SI and TIBC seemed to respond rapidly to the treatment within a week while Hb and Hct began to recover after 2 weeks of treatment (Table 3).

Regarding pregnancy outcome, there was no statistical difference between two groups in terms of GA at delivery and baby's birth weight (Table 4). Low birth weight (<2,500 g) infants were more common in the OFF-group without statistical significance (3 cases vs. 1 case; p = 0.30).

Concerning patient's compliance, all patients in the ISC-group received the complete dose of 500 mg iron while almost 100 % of participants in the OFF-group had followed the protocol. No serious adverse drug reactions were observed in both OFF and

Table 1. Patients' demographic data

Data	Total $(n = 80)$	ISC-group (n = 40)	OFF-group (n = 40)
Age (years)	24.6±5.4	24.3±4.9	24.9±5.9
Body weight (kg)	49.2±7.4	48.1±8.1	50.2±6.6
Body mass index (kg/m ²)	19.9±2.9	19.7±3.4	20.1±2.2
C-reactive protein (mg/L)	3.9±2.2	3.7±2.0	4.0±2.3

ISC, iron sucrose complex; OFF, oral ferrous fumarate

Table 2. Blood parameters and iron status at baseline, 36 weeks and at delivery

Characteristic	GA 32 w	vks (Baseline)		GA 36 wks			At Delivery		
	OFF-group $(n = 40)$	ISC-group (n = 40)	p-value	OFF-group (n = 36)	$\frac{\text{ISC-group}}{(n=38)}$	p-value	OFF-group (n = 25)	ISC-group (n = 25)	p-value
Hb (g/dL)	9.8 (9.3, 10.3)	9.8 (9.2, 10.2)	0.791	10.5	10.7	0.094	11.6 (10.3, 12.2)	11.5	0.757
Hct (%)	(9.5, 10.5) 30.9 (29.4, 31.7)	(9.2, 10.2) 30.1 (28.5, 30.9)	0.138	32.5 (31.2, 34.5)	32.6 (31.8, 34.0)	0.545	(10.3, 12.2) 35.0 (32.1, 37.1)	(11.0, 11.9) 35.3 (33.8, 36.8)	0.613
SF (µg/L)	7.7 (5.2, 8.8)	7.1 (5.3, 8.8)	0.644	26.2 (18.9, 38.1)	123.8 (90.4, 176.2)	< 0.001	28.3 (20.6, 38.9)	66.3 (32.6, 93.7)	< 0.001
SI (µg/dL)	11.0 (7.2, 19.0)	10.3 (7.8, 15.3)	0.381	18.5 (12.7, 29.7)	18.0 (14.1, 28.4)	0.834	20.9 (13.6, 29.9)	20.2 (13.9, 32.5)	1.000
TIBC (µg/dL)	108.2 (98.4, 118.2)	107.4 (94.9, 120.7)	0.519	92.8 (80.2, 102.0)	90.3 (77.0, 98.2)	0.285	92.3 (78.8, 106.3)	98.5 (93.1, 113.6)	0.252

ISC, iron sucrose complex; OFF, oral ferrous fumarate; Hb, hemoglobin; Hct, hematocrit; SF, serum ferritin; SI, serum iron; TIBC, total iron binding capacity

Data presented as medians (25th percentile, 75th percentile) Mann-Whitney U test was used for analysis

Table 3. Trend of blood parameters and iron status in both groups

Data	Baseline GA 32 wks			GA 34 wks			GA 35 wks			GA 36 wks		p-value
	OFF-group n = 10	ISC-group n = 10	p-value	OFF-group n = 10	ISC-group n = 10	p-value	OFF-group n = 10	ISC-group n = 10	p-value	OFF-group n = 10	ISC-group n = 10	
Hb (g/dL)	9.8 (8.7, 10.1)	10.0 (9.4, 10.4)	0.529	9.7 (9.1, 10.0)	9.9 (9.4, 10.4)	0.529	10.0 (9.0, 10.5)	10.2 (9.5, 10.8)	0.912	10.3 (9.6, 10.8)	10.6 (10.4, 11.1)	0.165
Hct (%)	30.2 (28.3, 31.5)	30.1 (29.0, 31.7)	0.912	30.1 (29.0, 32.0)	30.5 (29.0, 31.3)	0.684	32.3 (29.4, 33.8)	31.8 (30.7, 32.9)	0.393	32.6 (30.8, 34.4)	32.5 (31.5, 35.1)	0.796
SF (µg/L)	6.3 (3.1, 8.7)	6.8 (5.9, 10.9)	0.315	15.5 (8.4, 20.1)	106.3 (87.2, 137.8)	< 0.001	24.7 (13.5, 36.8)	160.7 (136.5, 202.9)	< 0.001	22.6 (13.2, 38.9)	166.5 (134.0, 205.6)	< 0.001
SI (µg/dL)	17.5 (10.7, 46.5)	15.3 (9.9, 18.4)	0.353	29.0 (18.4, 80.3)	31.0 (14.6, 40.1)	0.912	28.4 (19.2, 84.7)	37.9 (22.3, 55.4)	0.796	25.4 (20.9, 33.6)	32.6 (26.5, 37.6)	0.089
TIBC (µg/dL)	121.2 (112.1, 142.5)	112.3 (89.7, 128.2)	0.247	118.5 (89.2, 140.0)	109.7 (89.7, 126.6)	0.631	99.2 (86.5, 119.9)	117.7 (90.4, 137.9)	0.247	105.5 (93.4, 130.7)	95.0 (84.0, 109.8)	0.143

ISC, iron sucrose complex; OFF, oral ferrous fumarate; Hb, hemoglobin; Hct, hematocrit; SF, serum ferritin; SI, serum iron; TIBC, total iron binding capacity

Table 4. Pregnancy outcome at delivery

Characteristic	OFF-group (n = 25)	ISC-group (n = 25)	<i>p</i> -value
Gestational age at delivery (weeks) Birth weight (g) Low birth weight ^a (no)	39.0 ± 1.3 $3,060.4 \pm 454.7$ 3	39.2±1.6 3,066.0±328.1	0.363 0.48 0.297 ^b

ISC, iron sucrose complex; OFF, oral ferrous fumarate

^a birth weight <2,500 g

^b Pearson Chi-Square test



Fig. 1 Study flow chart.



Fig. 2 The change of hemoglobin level in both groups at 32, 36 weeks of gestation and at delivery. (OFF, oral ferrous fumarate; ISC, intravenous sucrose complex).



Fig. 3 The change of serum ferritin level in both groups at 32, 36 weeks of gestation and at delivery. (OFF, oral ferrous fumarate; ISC, intravenous sucrose complex).

ISC groups. Most patients in the OFF-group tolerated well to iron tablets. Only 2 cases of mild GI disturbances were noted and clinically improved by taking drug shortly after meals. In the ISC-group, there was one case of painless minimal extravasation. After weekly of close observation, the patient had only a tiny skin hyperpigmentation which completely faded away at delivery.

Discussion

Owing to remarkably increased iron needs over gestation (\approx 1,000 mg) which could not be met by only nutritional intake, 30-60 mg of elemental iron daily with or without additional micronutrients is usually provided for pregnant women. This is the supplementation assuming that the women have 500 mg of stored iron. However, 40% of women worldwide enter pregnancy with no storage iron⁽¹⁶⁾ and IDA remains the major health concern in pregnant women throughout the world. The low efficiency of oral iron may also be due to the poor compliance of the women arising from side effects or forgetfulness and poor absorption caused by other food interference^(17,18) or certain GI conditions.

To bypass these problems associated with oral iron intake, parenteral iron is an appropriate option. Data of intravenous iron sucrose given safely made it the parenteral iron of choice in the present study⁽⁵⁻⁹⁾. Ganzoni formula has been recommended to determine the total iron dose which is equal to prepregnancy weight [kg] x (target Hb-actual Hb)[g/L] x 0.24+500 mg⁽¹⁰⁾. The resulting dose is given in divided infusions every other day or every few days. According to the present data however, most of Thai anemic pregnant women were lightweight (BW 49.2±7.4 kg; BMI of 19.9 ± 2.9 kg/m²) and had mild degree of anemia (9.6±0.9 g/L). Therefore, the authors hypothesized that 500 mg of iron should be adequate for maternal iron storage replenishment. In addition, ISC administration protocol in the present study was modified into weekly infusions to be in line with routine antenatal appointment to improve patients' convenience.

With the present dosage and infusion protocol, the authors found that it took 2-3 weeks for the improvement of Hb and Hct to become discernible in both groups. At delivery, which was on average at 39 weeks' gestation for both groups (Table 4), the Hb and Hct levels continued to rise (Table 2 and Fig. 2). In the ISC-group, the rising of Hb and Hct appeared slower than that of serum ferritin which rapidly increased within a week post therapy. Serum ferritin level in the ISC-group escalated to very high peak within 2 weeks. Then, it started to decline but still remained significantly higher than that of the OFF- group at delivery (66.3 vs. 28.3 μ g/L). The change could be explained by its pharmacokinetics. After infused directly into the circulation, the blood level of ISC is high and is quickly uptaken in the reticuloendothelial system which is the storage site, mostly in the liver and the spleen, and subsequently released for bone marrow utilization⁽¹⁹⁾. On the other hand, about 12-25% of iron in the duodenum is gradually absorbed as transferrin-bound and other protein-bound iron into plasma iron pool^(4,16). This may result in a constantly low blood iron level, not high enough for storage purpose.

Thus, the present study showed that weekly ISC injection with the total dose of 500 mg in mild IDA pregnant women is effective to increase both Hb and Hct concentration in late pregnancy. The present infusion protocol is also proved to rapidly replenish maternal iron storage and beneficial to patients with preterm delivery risk. Similarly, a study from India also reported that anemic pregnant women at 24-34 weeks' gestation who received ISC had a higher Hb and serum ferritin than their counterpart who received oral iron⁽²⁰⁾. Another study in pregnancy at 32-35 weeks, also from India, revealed significant rise in Hb levels from baseline on days 14, 21, 28 and at delivery⁽²¹⁾. The calculated dose from Ganzoni formula was given in divided doses to be infused on alternate days in both studies and their patients were more anemic than patients in the present study.

In the present study, the increasing Hb and Hct levels were similar between two groups but this similarity was achieved by the women in the OFFgroup taking the oral iron tablets accurately. They were under strict surveillance and their compliance was indeed better than in the ordinary situation. However, serum ferritin levels differed significantly. A research group recently reported that in non-anemic pregnant women with routine oral iron supplementation, iron depletion was still found in the 1st, 2nd and 3rd trimesters at the prevalence of 20, 54 and 66% respectively⁽²²⁾. In the report, women with early antenatal iron depletion delivered baby weighing 192 g less than mothers with normal iron storage. This underlines the importance of iron storage even in the cases where anemia is absent. According to the present data, pregnancy outcomes in both groups were not different. Low birth weight infants were slightly more common in the OFF-group than the ISC-group, but there was no statistical significance. It is also of note that with similar rate of Hb and Hct rising, ISC could replenish the iron storage faster and in much more amount than OFF. This will

be beneficial if preterm labor took place.

A recent systematic review reported that intravenous iron sucrose, given to pregnant women, was associated with fewer side effects than regular oral iron therapy⁽²³⁾. In the present study, a few cases of mild GI discomfort in the OFF-group were observed and easily relieved while one case of mild extravasation with spontaneous resolution was found in the ISC group. No serious adverse events were noted. However, risk assessment for hypersensitivity reactions, appropriate rate of ISC administration in a facility where prompt recognition and treatment by welltrained staff are available, a test dosing for the first ISC administration, and close monitoring during and after each infusion should be performed to ensure patient safety⁽²⁴⁾. While no fatality had been reported from ISC treatment in an earlier review⁽²⁵⁾, a case of anaphylactic reaction to ISC leading to mortality in a pregnant woman was recently described from India⁽²⁶⁾.

Regarding the cost of treatment for each patient in the present study, ISC administration is about 8-10 times more expensive than oral iron supplementation. However, it is suitable for patients with the aforementioned problems of oral iron with better iron store replenishing.

Limitation of the present study: As the subjects were only mildly anemic and were lightweight, the results should be applied to the similar patients. Additional amount of iron may be required prior to or at delivery in cases of severe anemia or for heavy weight women. Moreover, the secondary results (at delivery) were based on only 25 patients in each group. However, the authors have looked into the characteristics of the patients whose data at delivery were not available and found that they were similar to the remaining patients. The authors consider that the comparison between groups at delivery is still applicable.

The strength of the study: Several parameters of iron status were used in the study and showed the same trends of changes.

In summary, 500 mg of ISC administered in 200-mg weekly divided doses is more efficacious in replenishing iron storage but not more efficacious in raising hemoglobin level compared with daily oral ferrous fumarate for pregnant women with IDA in late pregnancy.

What is already known on this topic?

Iron sucrose complex (ISC) can correct

anemia in pregnancy with the dose calculated by Ganzoni's formula and given every 2-3 days.

What this study adds?

ISC can be used in lower dose and infused in less frequency than the previous studies to replenish iron store for Thai anemic pregnant women who usually are lightweight and mildly anemic.

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Potential conflicts of interest

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การให้ไอออนซูโครสขนาดต่ำทางหลอดเลือดดำสัปดาห์ละครั้งเปรียบเทียบกับรับประทานยาธาตุเหล็กทุกวันสำหรับภาวะ เลือดจางจากการขาดธาตุเหล็กในระยะท้ายของการตั้งครรภ์: การศึกษาแบบสุ่ม

พรพิมล เรื่องวุฒิเลิศ, พฤหัส จันทร์ประภาพ, ประคอง ชื่นวัฒนา, วิทยา ถิฐาพันธ์, จุฬาลักษณ์ โกมลตรี

วัตถุประสงก์: เพื่อเปรียบเทียบประสิทธิศักย์ของการให้ไอออนซูโครสขนาดต่ำทางหลอดเลือดดำสัปดาห์ละครั้งกับยาธาตุเหล็กชนิด รับประทานสำหรับภาวะเลือดจางจากการขาดธาตุเหล็กในระยะท้ายของการตั้งครรภ์

วัสดุและวิธีการ: สตรีตั้งครรภ์เดี่ยวที่มีเลือดจางจากการขาดธาตุเหล็กที่อายุครรภ์ 33 สัปดาห์จำนวน 80 คน ถูกสุ่มให้ได้รับยาธาตุ เหล็กรับประทานวันละ 200 มิลลิกรัมจนคลอด (กลุ่มธาตุเหล็กรับประทาน) หรือได้รับไอออนซูโครสคอมเพล็กซ์ เข้าทางหลอด เลือดดำสัปดาห์ละ 1 ครั้ง ครั้งละ 200 มิลลิกรัม จนใด้ 500 มิลลิกรัม (กลุ่มธาตุเหล็กเข้าหลอดเลือดดำ) ประเมินผลเลือดทาง โลหิตวิทยาและภาวะธาตุเหล็กที่อายุครรภ์ 36 สัปดาห์ และเมื่อคลอด และบันทึกผลลัพธ์ของการตั้งครรภ์และผลข้างเคียงของยา ผลการศึกษา: มีการเพิ่มขึ้นของระดับฮีโมโกลบินอย่างช้า ๆ ในทั้งสองกลุ่มที่อายุครรภ์ 36 สัปดาห์และเมื่อคลอด ระดับซีรัมเฟอร์ ริตินในกลุ่มธาตุเหล็กเข้าหลอดเลือดดำสูงเป็น 4.7 เท่าของกลุ่มธาตุเหล็กรับประทานที่อายุครรภ์ 36 สัปดาห์[123.8 (90.4, 176.2) เทียบกับ 26.2 (18.9, 38.1) ใมโครกรัมต่อเดซิลิตร, p<0.001] และยังคงสูงเป็น 2.3 เท่า เมื่อคลอด [66.3 (32.6, 93.7) เทียบกับ 28.3 (20.6, 38.9) ใมโครกรัมต่อเดซิลิตร, p<0.001] ใม่พบผลข้างเคียงรุนแรง ทั้งสองกลุ่มมีน้ำหนักทารกแรกคลอด ใกล้เคียงกัน

สรุป: การให้ไอออนซูโครสคอมเพล็กซ์ขนาดต่ำทางหลอดเลือดดำแบ่งให้สัปดาห์ละ 1 ครั้ง มีประสิทธิศักย์ในการเพิ่มธาตุเหล็ก สะสมได้ดีกว่าการรับประทานยาธาตุเหล็ก (เฟอร์รัส ฟูมาเรท) ทุกวัน ในการรักษาภาวะเลือดจางจากการขาดธาตุเหล็กในระยะท้าย ของการตั้งครรภ์ อย่างไรก็ตามทั้งสองวิธีสามารถเพิ่มระดับฮีโมโกลบินได้ไม่ต่างกัน