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ORIGINAL PAPER

Ferric carboxymaltose for treatment of iron deficiency and iron deficiency anemia caused by abnormal uterine bleeding

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Abstract

Introduction: Heavy menstrual bleeding leads to depletion of iron stores, with subsequent iron deficiency (ID) and iron deficiency anemia (IDA). To evaluate the efficacy and safety of ferric carboxymaltose (FCM) in treatment of ID/IDA caused by abnormal uterine bleeding (AUB).

Material and methods: One hundred and twenty women ≥ 40 years old with chronic AUB and ID/IDA were included in this study for correction of ID/IDA. Participants received FCM infusion for correction of ID/IDA. The pre-treatment ferritin, hemoglobin (Hb), red blood cell (RBC) mean corpuscular volume (MCV), and RBC mean corpuscular hemoglobin (MCH) values were compared with the 6- and 12-week post-treatment values.

Results: The pre-treatment ferritin and Hb levels significantly increased from 13.2 ±7.4 µg/l and 8.8 ±0.8 g/dl, respectively, to 111.5 ±5.6 µg/l and 13.9 ±0.6 g/dl, respectively, 6 weeks after FCM (p = 0.001 and 0.0009; respectively), and to 98.7 ±6.1 µg/l and 12.9 ±0.65 g/dl, respectively, 12 weeks after FCM (p = 0.01 and 0.01; respectively). In addition, the pre-treatment RBC MCV and RBC MCH values significantly increased from 74.3 ±2.3 fl and 26.6 ±5.3 pg, respectively, to 88.7 ±1.9 fl and 29.6 ±4.5 pg, respectively, 6 weeks after FCM (p = 0.01 and 0.03, respectively), and to 93.3 ±1.75 fl and 30.3 ±3.8 pg, respectively, 12 weeks after FCM (p = 0.001 and 0.0001, respectively).

Conclusions: FCM was safe and effective for correction of ID/IDA caused by chronic AUB within 6 weeks. The serum ferritin, Hb, and RBC indices remained significantly high compared to the pre-treatment values 12 weeks after FCM infusion.

Key words: ferric carboxy maltose (FCM), iron deficiency (ID), iron deficiency anemia (IDA), abnormal uterine bleeding (AUB).

Introduction

Women with heavy menstrual bleeding (HMB) lose 5–6 times more iron per cycle than those with normal menses [1]. Heavy menstrual bleeding leads to iron store depletion with subsequent iron deficiency (ID) [1, 2].

About two-thirds of the body's iron is bound to hemoglobin (Hb) within the red blood cells (RBCs), and severe ID can subsequently lead to microcytic hypochromic iron deficiency anemia (IDA) [3].

Mild IDA can be asymptomatic, while symptomatic IDA can present with weakness, fatigue, headache, hair loss, brittle nails, and shortness of breath [3, 4]. Iron deficiency anemia can significantly reduce the quality of life, cognitive ability, and work productivity [5].

Evaluation of abnormal uterine bleeding (AUB) in women ≥ 40 years is crucial to exclude endometrial carcinoma. Dilatation and curettage (D&C) is the gold standard for endometrial sampling in AUB [6, 7].

Preoperative IDA is a risk factor for postoperative morbidity, including infection, prolonged hospital stays, and blood transfusion [1].

In addition, the risks associated with preoperative IDA were not eliminated by blood transfusions [8], and the preoperative transfusion corrects only the anemia (not the underlying cause) [9–11].

Studies have shown that correction of IDA prior to surgery reduces the postoperative blood transfusion, and improves the hematological parameters [12, 13].

Effective correction of ID/IDA in women with AUB improves the quality of life [14], while preoperative intravenous (IV) iron reduces the postoperative anemia and postoperative blood transfusion compared to no treatment [15].

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Iron sucrose (IS) was approved in the United States and Europe for treatment of ID/IDA. The multiple infusion sessions are the main disadvantage of IS [11]. Ferric carboxymaltose (FCM) is a new IV iron, which can be used for correction of ID/IDA when there is clinical need to deliver iron for correction of ID/IDA rapidly. Froessler *et al.* found that FCM infusion significantly increased the Hb levels of pregnant women at 3, 6, and 8 weeks after infusion [16], and a randomized control trial (RCT) found that FCM was tolerable and effective for rapid correction of postpartum anemia [17]. Therefore, this study was designed to evaluate the efficacy and safety of FCM in treatment of ID/IDA caused by AUB.

Material and methods

One hundred and twenty women ≥ 40 years old with chronic AUB and ID/moderate IDA were included in this cohort study for correction of ID/IDA before D&C.

This study was conducted over one year (December 2019 to December 2020). Participants were included in this study after informed consent in accordance with the Helsinki Declaration, and after approval of the FCM for treatment of ID/IDA by the hospital's drug committee.

Chronic AUB is defined as frequent uterine bleeding (recurs within < 24 days) over the last 6 months, > 80 ml in amount, and lasting > 8 days [18].

The International Federation of Gynecology and Obstetrics PALM-COEIN (polyp, adenomyosis, leiomyoma, malignancy including hyperplasia – coagulopathy, ovulatory, endometrial, iatrogenic, and not otherwise classified) classification of AUB facilitated accurate diagnosis and treatment. PALM defined the structural causes of AUB while COEIN defined the non-structural (functional) causes of AUB [18].

The Royal College of Obstetricians and Gynaecologists, and the American College of Obstetricians and Gynecologists prefer the patient-centered definition of HMB as excess menstrual blood loss which interferes with the women's physical and social life and/or quality of life, and necessitates investigation and treatment [18]. The pictorial blood loss assessment chart was used in this study to assess the menstrual blood loss [19].

The diagnosis of ID was based on serum ferritin (< 30 µg/l), and the diagnosis of moderate IDA was based on serum ferritin (< 30 µg/l), Hb concentration (≥ 8 and < 12 g/dl), RBC mean corpuscular volume (MCV < 80 fl), and RBC mean corpuscular hemoglobin (MCH < 27 pg) [20–22].

Iron deficiency anemia in non-pregnant women was classified according to the WHO definition into severe anemia when Hb < 8 g/dl, moderate anemia ≥ 8 Hb < 12 g/dl, and mild anemia ≥ 11 Hb < 12 g/dl [20].

Participants were evaluated thoroughly and subjected to transvaginal ultrasound (TVS) examination followed by laboratory investigation including serum ferritin (using UniCel DxI 800 analyzer, Beckman Coulter Inc., USA), complete blood count (using UniCel DxH 800 hematology analyzer, Beckman Coulter Inc., USA), coagulation profile [i.e., clotting, bleeding and activated partial thromboplastin (APTT) times], prolactin and thyroid hormones [using enzyme linked immunoassay (ELISA)], and liver function tests (i.e., alanine transaminase and aspartate transaminase using Synchron LX20, Beckman Coulter Inc., USA).

The transvaginal ultrasound was done for all participants by an expert sonographer blind to participants' data (to avoid potential bias). The endometrium was evaluated in sagittal and axial planes for its thickness (uniform or localized thickness) and regularity. The normal atrophic postmenopausal endometrium appears thin and homogeneous [23]. Based on the current state of knowledge and cited diagnostic methodology, thickened endometrium is often indicative of endometrial pathology [23]. The presence of an endometrial complex favors a focal intracavitary process (i.e., polyp, or focal endometrial hyperplasia). The myometrium is also evaluated regarding its thickness, regularity, and contour [23].

Women included in this study were ≥ 40 years old (premenopausal or postmenopausal), diagnosed as chronic AUB associated with ID/moderate IDA, euthyroid, with normal prolactin, and liver function tests, normal bleeding, clotting, APTT times, and platelet count [6, 7].

Women with acute AUB (necessitates immediate action), intolerance or hypersensitivity to iron preparations, severe IDA, and/or anemia other than IDA [20–22], possibility of pregnancy, endocrine disturbance (i.e., hyperprolactinemia or thyroid disorders), history of contraception, and/or hormonal replacement therapy (HRT) were excluded from this study [20–22].

Ferric carboxymaltose (Ferinject 50 mg iron/ml solution, Vifor Pharma, UK) is approved for treatment of ID/IDA when oral iron preparations are ineffective, contraindicated or when there is clinical need to deliver iron for correction of ID/IDA rapidly. The effect of FCM on IDA should not be assessed before 4 weeks after the last FCM infusion to allow adequate time for erythropoiesis, and iron utilization.

The needed iron dose of FCM to correct the ID/IDA was calculated when Hb was < 10 gm/dl according to participants` body weight: 500 mg of iron (< 35 kg), 1500 mg of iron (> 35 < 70 kg), and 2000 mg of iron (> 70 kg).

The calculated iron dose of FCM was diluted in 100 mL of 0.9% normal saline over 6 min when it was ≥ 500 mg, and in 250 mL of 0.9% normal saline over 15 min when it was > 500–1000 mg.

The total iron infusion dose of FCM should not exceed 20 mg iron/kg body weight, and the maximum recommended iron infusion dose of FCM was 1000 mg of

iron/week. More than 1000 mg of iron was given in two infusion sessions [1000 mg in the first session, and the remaining amount in the second session (the two sessions scheduled one week apart)].

Participants were observed during the FCM infusion, and for at least 30 min following FCM infusion for signs of anaphylaxis, intolerance, and/or side effects (skin eruption, tachycardia, headache, abdominal or chest pain) to evaluate the safety of FCM (secondary outcome).

Participants also received oral folic acid tablets for 12 weeks to avoid folate deficiency. The pre-treatment ferritin, Hb, RBC MCV, and RBC MCH values were compared with the 6- and 12-week post-treatment values to evaluate the efficacy of FCM in treatment of ID/IDA caused by chronic AUB (primary outcome).

Sample size

The required sample size was calculated using G Power software version 3.1.9.7 for sample size calculation (Heinrich Heine Universität, Düsseldorf, Germany), setting α – error probability at 0.05, power (1-β error probability) at 0.95% and effective sample size (w) at 0.5. An effective sample of ≥110 women was needed to produce a statistically acceptable figure.

Statistical analysis

Collected data were statistically analyzed using SPSS version 20 (Chicago, IL, USA). The mean and standard deviation (±SD) were used to present numerical values, while the number (N) and percentage (%) were used to present categorical values. Student's t-test was used to compare the pre-treatment ferritin, Hb, RBC MCV, and RBC MCH values by the 6- and 12-week post-treatment values to detect the efficacy of FCM in treatment of ID/IDA caused by chronic AUB. A p-value < 0.05 was considered significant when the Student's t-test was used to compare the pre-treatment values with the 6- and 12-week post-treatment values.

Participants were included in this study after informed consents in accordance with the Helsinki Declaration, and after approval of the FCM for treatment of ID/IDA by the hospital's drug committee.

Results

One hundred and twenty women ≥ 40 years old with chronic AUB and ID/moderate IDA were included in this study for correction of ID/IDA before D&C using FCM. The pre-treatment ferritin, Hb, RBC MCV, and RBC MCH values were compared with the 6- and 12-week post-treatment values to evaluate the efficacy of FCM in treatment of ID/IDA caused by chronic AUB. Participants were observed during the FCM infusion, and for at least 30 min following FCM infusion for signs of anaphylaxis, intolerance, and/or side effects to evaluate the safety of FCM.

Table 1. Demographic data of participants, possible causes of abnormal uterine bleeding and pre-treatment ferritin, hemoglobin, red blood cell mean corpuscular volume and red blood cell mean corpuscular hemoglobin values

Parameters	Studied women with chronic AUB and ID/IDA (n = 120)
Age (years)	45.4 ±2.6
Parity	3.5 ±2.4
Maternal weight [kg]	82.3 ±7.5
Total required iron dose [mg]	1506.3 ±166.5
Causes of AUB (%)	
AUB-O	59 (49.2)
AUB-P	23 (19.2)
AUB-L	19 (15.8)
AUB-A	9 (7.5)
AUB-E	7 (5.8)
AUB-C	3 (2.5)
Pre-treatment ferritin [µg/l]	13.2 ±7.4
Pre-treatment Hb [g/dl]	8.8 ±0.8
Pre-treatment RBC MCV [fl]	74.3 ±2.3
Pre-treatment RBC MCH [pg]	26.6 ±5.3

A – adenomyosis, AUB – abnormal uterine bleeding, C – coagulopathy, E – endometrium, Hb – hemoglobin, ID – iron deficiency, IDA – iron deficiency anemia, L – leiomyoma, MCH – mean corpuscular hemoglobin, MCV – mean corpuscular volume, N – number of patients, O – ovulatory, P – polyp, RBC – red blood cell
Data are presented as mean ± standard deviation and number and percentage (%).

Table 1 shows the demographic data of participants, possible causes of AUB based on thorough evaluation (including history, TVS and laboratory findings), and pre-treatment ferritin, Hb, RBC MCV, and RBC MCH values.

The pre-treatment ferritin and Hb levels significantly increased from 13.2 ±7.4 µg/l and 8.8 ±0.8 g/dl, respectively, to 111.5 ±5.6 µg/l and 13.9 ±0.6 g/dl, respectively, 6 weeks after FCM (p = 0.001 and 0.0009, respectively). Also, the pre-treatment RBC MCV and RBC MCH values significantly increased from 74.3 ±2.3 fl and 26.6 ±5.3 pg, respectively, to 88.7 ±1.9 fl and 29.6 ±4.5 pg, respectively, 6 weeks after FCM (p = 0.01 and 0.03 respectively) (Table 2).

The pre-treatment ferritin and Hb levels significantly increased from 13.2 ±7.4 µg/l and 8.8 ±0.8 g/dl, respectively, to 98.7 ±6.1 µg/l and 12.9 ±0.65 g/dl, respectively, 12 weeks after FCM (p = 0.01 and 0.01, respectively). Also, the pre-treatment RBC MCV and RBC MCH values significantly increased from 74.3 ±2.3 fl and 26.6 ±5.3 pg, respectively, to 93.3 ±1.75 fl and 30.3 ±3.8 pg, respec-

Table 2. Pre-treatment ferritin, hemoglobin, red blood cell mean corpuscular volume and red blood cell mean corpuscular hemoglobin values compared to the 6-week post-treatment values

Variables	Pre-treatment values (n = 120)	6-week post-treatment values (n = 120)	p-value (95% CI)
Pre-treatment ferritin [µg/l]	13.2 ±7.4	111.5 ±5.6	0.001* (–99.97, –98.3, –96.63)
Pre-treatment Hb [g/dl]	8.8 ±0.8	13.9 ±0.6	0.0009* (–5.3, –5.1, –4.9)
Pre-treatment RBC MCV [fl]	74.3 ±2.3	88.7 ±1.9	0.01* (–14.94, –14.4, –13.9)
Pre-treatment RBC MCH [pg]	26.6 ±5.3	29.6 ±4.5	0.03* (–4.3, –3, –1.75)

CI – confidence interval, Hb – hemoglobin, MCH – mean corpuscular hemoglobin, MCV – mean corpuscular volume, N – number of patients, p – the p-value when the pre-treatment value was compared to the 6-week post-treatment value using Student's t-test, RBC – red blood cell, * significant difference
Data are presented as mean ± standard deviation.

Table 3. Pre-treatment ferritin, hemoglobin, red blood cell mean corpuscular volume and red blood cell mean corpuscular hemoglobin values compared to the 12-week post-treatment values

Variables	Pre-treatment values (n = 120)	12-week post-treatment values (n = 120)	p-value (95% CI)
Pre-treatment ferritin [µg/l]	13.2 ±7.4	98.7 ±6.1	0.01* (–87.2, –85.5, –83.78)
Pre-treatment Hb [g/dl]	8.8 ±0.8	12.9 ±0.65	0.01* (–4.3, –4.1, –3.9)
Pre-treatment RBC MCV [fl]	74.3 ±2.3	93.3 ±1.75	0.001* (–19.5, –19, v18.48)
Pre-treatment RBC MCH [pg]	26.6 ±5.3	30.3 ±3.8	0.0001* (–4.87, –3.7, –2.53)

CI – confidence interval, Hb – hemoglobin, MCH – mean corpuscular hemoglobin, MCV – mean corpuscular volume, N – number of patients, p – p-value when the pre-treatment value was compared to the 12-week post-treatment value using Student's t-test, RBC – red blood cell, * significant difference
Data are presented as mean ± standard deviation.

tively, 12 weeks after FCM (p = 0.001 and 0.0001, respectively) (Table 3).

No anaphylaxis and/or intolerance to FCM was reported in this study, the only reported side effects were burning sensation at the infusion site [1.66% (2/120)] and mild headache during the infusion [0.83% (1/120)].

Discussion

The causes of chronic AUB in this study based on thorough evaluation (i.e., history, TVS and laboratory findings) were AUB-O (49.2%), AUB-P (19.2%), AUB-L (15.8%), AUB-A (7.5%), AUB-E (5.8%), and AUB-C (2.5%).

Similarly, Sun et al. studied the prevalence of chronic AUB causes among Chinese women using the PALM-COEIN classification system, and found that AUB-O was the most frequent cause of chronic AUB (57.7%), followed by AUB-P (16.2%), AUB-L (12%), AUB-A (4.94%), AUB-E (2%), and AUB-C (1%) [24].

AUB-O is commonly observed at the extremes of reproductive age, and commonly associated with endocrine disorders (i.e., hyperprolactinemia, hypothyroidism), obesity, and/or weight loss [18].

Whitaker *et al.* [18] found that the incidence of uterine polyps in chronic AUB varies widely among studies (3.7–65%), and this difference can be explained by the inclusion criteria and number of studied women [25].

Although > 50% of women with uterine fibroids are asymptomatic, some uterine fibroids can present with chronic AUB and ID/IDA [24]. The reported incidence of uterine fibroids as a cause of chronic AUB in this study was 15.8%, and was 12% in the Sun *et al.* study [24]. Similarly, Fraser *et al.* [26] and Shapley *et al.* [27] reported uterine fibroids (AUB-L) as a possible cause of AUB in 14–25% of women.

Although the reported incidence of adenomyosis as a cause of chronic AUB was 7.5% in this study, and was 4.94% in the Sun *et al.* study [24], Morassutto *et al.* reported a 20–30% prevalence for adenomyosis in AUB [28]. Morassutto *et al.* explained this difference by the diagnostic criteria (histological and radiological) used for diagnosis of adenomyosis [28].

The diagnosis of AUB-E depends on a careful history, and exclusion of other causes. The lack of available biomarkers for diagnosis of endometrial disorders indicates that the incidence of endometrial disorders in AUB (AUB-E) is underestimated [18].

Coagulopathies affect 13% of the women with HMB [18], and anticoagulants and antiplatelets have been considered as a part of AUB-C (rather than AUB-I) [18].

Iron deficiency anemia can significantly reduce the quality of life, cognitive ability, and work productivity [5]. Preoperative IDA is a risk factor for postoperative morbidity, including infection, prolonged hospital stays, and blood transfusion [1]. Correction of IDA prior to surgery reduces the post-operative blood transfusions, and improves the hematological parameters [8, 9].

Conventional iron salts (ferrous salts) are associated with gastric discomfort, vomiting, and constipation, which adversely affect compliance [29].

Iron sucrose was approved in the United States and Europe for treatment of ID/IDA. The reported incidence of anaphylaxis with IS is low (0.002%), and there are no hypersensitivity reactions reported with IS [29]. The multiple infusion sessions are the main disadvantage of IS (200 mg of IS in each session every other day) [11, 22].

Ferric carboxymaltose is a new IV iron, which can be used for correction of ID/IDA when oral iron preparations are ineffective, contraindicated or when there is a clinical need to deliver iron for correction of ID/IDA rapidly. Therefore, this study was designed to evaluate the efficacy and safety of FCM in treatment of ID/IDA caused by AUB. In the study, the pre-treatment ferritin and Hb levels significantly increased from 13.2 ±7.4 µg/l and 8.8 ±0.8 g/dl, respectively, to 111.5 ±5.6 µg/l and 13.9 ±0.6 g/dl, respectively, 6 weeks after FCM (p = 0.001 and 0.0009, respectively), and to 98.7 ±6.1 µg/l and 12.9 ±0.65 g/dl, respectively, 12 weeks after FCM (p = 0.01 and 0.01, respectively).

In addition, the pre-treatment RBC MCV and RBC MCH values significantly increased from 74.3 ±2.3 fl and 26.6 ±5.3 pg, respectively, to 88.7 ±1.9 fl and 29.6 ±4.5 pg, respectively, 6 weeks after FCM (p = 0.01 and 0.03, respectively), and to 93.3 ±1.75 fl and 30.3 ±3.8 pg, respectively, 12 weeks after FCM (p = 0.001 and 0.0001, respectively).

A systematic review found that IV iron is a safe alternative to address the problem of ID in women who require rapid replacement of iron stores [30].

An RCT found IV iron beneficial for pregnant women who presented with anemia at later gestation when rapid replacement of iron stores was required [31].

Froessler *et al.* studied the safety and efficacy of FCM in treatment of IDA during pregnancy, and found that FCM infusion significantly increased the Hb levels in all studied women at 3, 6, and 8 weeks after infusion. Froessler *et al.* reported minor side effects in 20% of studied women [16].

The reported side effects with FCM infusion in this study were burning sensation at the infusion site (1.66%) and mild headache during FCM infusion (0.83%).

An RCT was conducted by Van Wyck *et al.* to evaluate the effect of FCM infusion (≤1000 mg over 15 min) for treatment of postpartum anemia. Van Wyck *et al.* found that FCM was tolerable and effective for rapid correction of postpartum anemia [17].

Another RCT found that FCM infusion improved the iron stores of pregnant women with significant elevation of Hb levels within 12 weeks compared to IS. The convenient dosing and fewer infusion sessions result in better patient compliance with FCM infusion [32].

Overall, there is substantial evidence that FCM is effective in treating IDA in many acute and chronic conditions, with a favorable benefit-risk profile [33].

This study found that the pre-treatment ferritin and Hb levels significantly increased 6 and 12 weeks after FCM infusion. In addition, the pre-treatment RBC MCV and RBC MCH values significantly increased 6 and 12 weeks after FCM infusion. The only reported side effects with FCM infusion were burning sensation at the infusion site (1.66%) and mild headache during FCM infusion (0.83%).

This study concluded that the FCM was safe and effective for correction of ID/IDA caused by chronic AUB within 6 weeks. The serum ferritin and Hb levels and the RBC indices remained significantly high compared to the pre-treatment values 12 weeks after FCM infusion.

This study was the first cohort study conducted to evaluate the efficacy and safety of FCM in treatment of ID/IDA in women with chronic AUB.

Women who refused to participate and absence of postoperative follow-up after D&C were the limitations of this study. Further future studies comparing the efficacy and safety of FCM with other IV iron preparations including IS are needed.

Conclusions

Ferric carboxymaltose was safe and effective for correction of ID/IDA caused by chronic AUB within 6 weeks. The serum ferritin and Hb levels and the RBC indices remained significantly high compared to the pre-treatment values 12 weeks after FCM infusion.

Disclosure

The authors report no conflict of interest.

References

1. Mansour D, Hofmann A, Gemzell-Danielsson K. A review of clinical guidelines on the management of iron deficiency and iron-deficiency anemia in women with heavy menstrual bleeding. Adv Ther 2021; 38: 201-225.
2. Camaschella C. Iron-deficiency anemia. N Engl J Med 2015; 372: 1832-1843.
3. American College of Obstetricians and Gynecologists. ACOG Practice Bulletin No. 95: anemia in pregnancy. Obstet Gynecol 2008; 112: 201-207.
4. Percy L, Mansour D, Fraser I. Iron deficiency and iron deficiency anaemia in women. Best Pract Res Clin Obstet Gynaecol 2017; 40: 55-67.
5. Froessler B, Gajic T, Dekker G, Hodyl NA. Treatment of iron deficiency and iron deficiency anemia with intravenous ferric carboxymaltose in pregnancy. Arch Gynecol Obstet 2018; 298: 75-82.
6. Abdelazim IA, Aboelezz A, Abulkareem AF. Pipelle endometrial sampling versus conventional dilatation & curettage in patients with abnormal uterine bleeding. J Tur Ger Gynecol Assoc 2013; 14: 40-49.
7. Abdelazim IA, Abdelrazak KM, Elbiaa AA, Al-Kadi M, Yehia AH. Accuracy of endometrial sampling compared to conventional dilatation and curettage in women with abnormal uterine bleeding. Arch Gynecol Obstet 2015; 291: 1121-1126.
8. Richards T, Musallam KM, Nassif J, et al. Impact of preoperative anaemia and blood transfusion on postoperative outcomes in gynaecological surgery. PLoS One 2015; 10: e0130861.
9. Abdelazim IA, Nusair B, Svetlana S, Zhurabekova G. Treatment of iron deficiency and iron deficiency anemia with intravenous ferric carboxymaltose in pregnancy. Arch Gynecol Obstet 2018; 298: 1231-1232.
10. Abdelazim IA, Shikanova S, Karimova B, Sarsembayev M, Mukhambetalyeva G. Heme-iron optifer versus intravenous iron/ferosac in treatment of iron efficiency anemia during pregnancy. SN Compr Clin Med 2021; 3: 1344-1349.
11. Abdelazim IA, Abu-Faza M, Shikanova S, Zhurabekova G, Maghrabi MM. Heme-bound iron in treatment of pregnancy-associated iron deficiency anemia. J Family Med Prim Care 2018; 7: 1434-1438.
12. Spahn DR, Schoenrath F, Spahn GH, et al.. Effect of ultra-short-term treatment of patients with iron deficiency or anaemia undergoing cardiac surgery: a prospective randomised trial. Lancet 2019; 393: 2201-2212.

13. Triphaus C, Judd L, Glaser P, et al.. Effectiveness of preoperative iron supplementation in major surgical patients with iron deficiency: a prospective observational study. Ann Surg 2021; 274: e212-e219.
14. Vaucher P, Druais PL, Waldvogel S, Favrat B. Effect of iron supplementation on fatigue in nonanemic menstruating women with low ferritin: a randomized controlled trial. CMAJ 2012; 184: 1247-1254.
15. Diez-Lobo AI, Fisac-Martín MP, Bermejo-Aycar I, MuÑOz M. Preoperative intravenous iron administration corrects anemia and reduces transfusion requirement in women undergoing abdominal hysterectomy. Transfus Altern Transfus Med 2007; 9: 114-119.
16. Froessler B, Collingwood J, Hodyl NA, Dekker G. Intravenous ferric carboxymaltose for anaemia in pregnancy. BMC Pregnancy Childbirth 2014; 14: 115.
17. Van Wyck DB, Martens MG, Seid MH, Baker JB, Mangione A. Intravenous ferric carboxymaltose compared with oral iron in the treatment of postpartum anemia: a randomized controlled trial. Obstet Gynecol 2007; 110: 267-278.
18. Whitaker L, Critchley HO. Abnormal uterine bleeding. Best Pract Res Clin Obstet Gynaecol 2016; 34: 54-65.
19. Magnay JL, O'Brien S, Gerlinger C, Seitz C. Pictorial methods to assess heavy menstrual bleeding in research and clinical practice: a systematic literature review. BMC Womens Health 2020; 20: 24.
20. Abdelazim IA, Farghali M, Amer O. Ferric polymaltose complex in treatment of iron deficiency and iron-deficiency anaemia with pregnancy. Hematology 2020; 11: 212-218.
21. Kanshaiym S, Zhurabekova G, Abdelazim IA, Starchenko T. Intravenous ferric carboxymaltose for the treatment of iron deficiency anemia: letter to editor. Hematol Transfus Cell Ther 2020; 42: 98-99.
22. Kanshaiym S, Abdelazim IA, Starchenko T, Mukhambetalyeva G. Effect of intravenous iron sucrose on hemoglobin level, when administered in a standard dose, to anemic pregnant women in rural Northern India. J Family Med Prim Care 2019; 8: 769-770.
23. Mandakini P, Anand P. Peri-and postmenopausal uterine bleeding transvaginal ultrasound with hysterosonography and diagnostic correlation with hysteroscopy. Ultrasound Obstet Gynecol 2011; 5: 343-352.
24. Sun Y, Wang Y, Mao L, Wen J, Bai W. Prevalence of abnormal uterine bleeding according to new International Federation of Gynecology and Obstetrics classification in Chinese women of reproductive age: a cross-sectional study. Medicine (Baltimore) 2018; 97: e11457.
25. Dreisler E, Stampe Sorensen S, Ibsen PH, Lose G. Prevalence of endometrial polyps and abnormal uterine bleeding in a Danish population aged 20–74 years. Ultrasound Obstet Gynecol 2009; 33: 102-108.
26. Fraser IS, Langham S, Uhl-Hochgraeber K. Health-related quality of life and economic burden of abnormal uterine bleeding. Expert Rev Obstet Gynecol 2009; 4: 179e89.
27. Shapley M, Jordan K, Croft PR. An epidemiological survey of symptoms of menstrual loss in the community. Br J Gen Pract 2004; 54: 359-363.
28. Morassutto C, Monasta L, Ricci G, Barbone F, Ronfani L. Incidence and estimated prevalence of endometriosis and adenomyosis in northeast Italy: a data linkage study. PLoS One 2016; 11: e0154227.
29. Khalafallah AA, Dennis AE. Iron deficiency anaemia in pregnancy and postpartum: pathophysiology and effect of oral versus intravenous iron therapy. J Pregnancy 2012; 2012: 630519.
30. Radhika AG, Sharma AK, Perumal V, et al.. Parenteral versus oral iron for treatment of iron deficiency anaemia during pregnancy and postpartum: a systematic review. J Obstet Gynaecol India 2019; 69: 13-24.
31. Gupta A, Manaktala U, Rathore AM. A randomized controlled trial to compare intravenous iron sucrose and oral iron in treatment of iron deficiency anemia in pregnancy. Indian J Hematol Blood Transfus 2014; 30: 120-125.
32. Jose A, Mahey R, Sharma JB, et al.. Comparison of ferric Carboxymaltose and iron sucrose complex for treatment of iron deficiency anemia in pregnancy – randomised controlled trial. BMC Pregnancy Childbirth 2019; 19: 54.
33. Muñoz M, Martín-Montañez E. Ferric carboxymaltose for the treatment of iron-deficiency anemia. Expert Opin Pharmacother 2012; 13: 907-921.