Doi: 10.5152/TJAR.2020.484

Original Article
Obstetric Anaesthesia

Turkish Journal of Anaesthesiology & Reanimation

Retrospective Evaluation of Effects of Preoperative Anaemia Treatment in Gynaecological and Obstetric Surgical Patients

Berrin Günaydın[1], Gizem Işık[2], Selin Bağcaz[1], Gözde İnan[1], Nuray Bozkurt[2], Zübeyde Nur Özkurt[3], M. Anıl Onan[2]

[1]Department of Anaesthesiology and Reanimation, Gazi University School of Medicine, Ankara, Turkey
[2]Department of Obstetrics and Gynecology, Gazi University School of Medicine, Ankara, Turkey
[3]Department of Hematology, Gazi University School of Medicine, Ankara, Turkey

Cite this article as: Günaydın B, Işık G, Bağcaz S, İnan G, Bozkurt N, Özkurt ZN, et al. Retrospective Evaluation of Effects of Preoperative Anaemia Treatment in Gynaecological and Obstetric Surgical Patients. Turk J Anaesthesiol Reanim 2021; 49(1): 25-9.

Abstract

Objective: In anemic patients undergoing surgery, there is an increase in the requirement of blood transfusion, longer hospital stay and higher intensive care unit adimission. In this study we aimed to evaluate the efficacy of iv iron treatment before elective obstetric or gynecological operations retrospectively.
Methods: After obtaining approval of ethics committee, records of 5688 patients underwent either obstetric or gynecological surgery between January 1st of 2016 to December 31st of 2018 were documented retrospectively and 241 anemic cases were identified. Eighty-one anemic patients who did not receive any iv iron treatment preoperatively were excluded and 160 cases treated with either iv iron (either sucrose or ferric carboxy maltose) were included. The laboratory results including haemoglobin (Hb), MCV,MCH and serum iron binding capacities, ferritin, iron and transferrin levels were documented before (preoperative) and after iv iron treatment (postoperative 10th day) were collected from files. Difference between preoperative and postoperative Hb, MCV, MCH, TIBC, serum ferritin, iron and transferrin levels of these cases were determined.
Results: In 97 obstetric cases, the differences of Hb, MCV, MCH, serum iron, ferritin, iron binding capacity values before surgery and postoperative 10th day were respectively found as 1.3 g dL^{-1} (p=0.000); 1.9 fL (p=0.000); 0.3 pg (p=0.01); 44.4 µg dL^{-1} (p=0.008); 85.9 µg L^{-1} (p=0.009); 211.7 µg dL^{-1} (p=0.001). In 63 gynecologic cases, same measurements were evaluated and similar differences in Hb, MCV, MCH, serum ferritin and transferrin saturation values were 1.25 g dL^{-1} (p=0.000); 2.2 fL (p=0.000); 0.8 pg (p=0.000); 215.6 µg L^{-1} (p=0.002); 41.5% (p=0.044). Two obstetric patients and 7 gynaecologic patients were transfused erytrocyte suspensions after surgery.
Conclusion: Efficacy of preoperative iv iron therapy in gynaecologic-obstetric patients with IDA has been demonstrated and its importance has been revisited once again.
Keywords: Anemia, iv iron treatment, obstetric and gynecologic surgeries, postoperative results

Introduction

World Health Organization (WHO) has reported nearly 2 billion people with anaemia across the globe. Of these, 32 million are pregnant women, and half of them have iron deficiency anaemia (IDA) (1). According to WHO, the definition of anaemia is based on the haemoglobin (Hb) concentration of less than 12 g dL^{-1} in women and less than 13 g dL^{-1} in men. However, reference Hb concentration for anaemia in pregnant women changes according to the gestation period of the pregnancy. The Hb concentration is less than 11 g dL^{-1}, 10.5 g dL^{-1} and 10 g dL^{-1} during the 1st, 2nd and 3rd trimester, respectively (2). Both mean corpuscular volume (MCV) <60 fL and mean corpuscular Hb (MCH)<280 pg L^{-1} in the total blood count support hypochromic microcytic anaemia. However, the total blood count is not enough for the diagnosis of anaemia; the aetiology should also be defined. Serum ferritin level under 15–20 µg L^{-1} and also serum iron levels, total iron-binding capacity (TIBC), transferrin saturation, reticulocyte count and C-reactive protein levels are important parameters in the differential diagnosis (2).

IDA is the most common type of anaemia in adults, and the symptoms include exhaustion, fatigue and palpitation. Gestational anaemia may cause maternal, foetal or neonatal adverse effects. Preterm delivery, stillbirth, placental abnor-

Corresponding Author: Gizem Işık E-mail: gizemgizem87@gmail.com

Received: 19.03.2020 Accepted: 13.05.2020
Available Online Date: 19.06.2020

malities, low birth weight, intrauterine growth retardation, premature rupture of membranes or chorioamnionitis are more common and increase the risk of perinatal mortality (3, 4).

In the general population, preoperative anaemia incidence can vary between 30% and 40%. According to the data of the United States, the preoperative anaemia rate is 26.5% for women and 31% for men. Indeed, anaemia prevalence was reported to be higher in women than in men until the age of 64 years; after this age, the anaemia incidence increases in men (5). Preoperative anaemia is associated with an increasing risk of mortality, major morbidity and requirement for blood transfusions. Blood transfusion may result in a higher risk of transfusion-related acute lung injury, transfusion-associated circulatory overload, renal failure, cerebrovascular events and myocardial infarction along with tumour growth factor and non-Hodgkin lymphoma development. Thus, increased morbidity and/or mortality may occur because of longer hospital stay and increased intensive care unit admission (6).

The guideline of the European Society of Anaesthesiology (ESA) on perioperative blood management and Network for the Advancement of Patient Blood Management, Haemostasis and Thrombosis (NATA) reports have consensus about treating pregnant women with intravenous (IV) iron in the case of severe anaemia (Hb<8 g dL^{-1}) that cannot be corrected within 2–4 weeks with oral iron or when the anaemia diagnosis is made later than 34 weeks of pregnancy (7, 8). Because of the symptoms and outcomes of IDA and the postoperative complications along with the great importance of treatment of patients with anaemia before the surgery, we aimed to evaluate the efficacy of IV iron treatment before elective obstetric and gynaecological operations retrospectively.

Methods

After obtaining approval of Institutional Gazi University ethics committee of clinical trials (Decision number 830, date 12.11.2018), the records of 5,688 patients who underwent either obstetric or gynaecological surgery between 1st January 2016 and 31st December 2018 were documented retrospectively from our hospital's general patient registry tracking system, and 241 anaemia cases were identified. Furthermore, 81 patients with anaemia who did not receive any IV iron treatment preoperatively were excluded and 160 patients treated with either IV iron sucrose (Venofer 100 mg/5 mL, IV injection, Abdi İbrahim, İstanbul) or ferric carboxy maltose (FCM) (Ferinject flakon 500 mg, Abdi İbrahim-Vifor Pharma) were included. Differences between the preoperative and postoperative Hb, MCV, MCH, TIBC, serum ferritin and iron and transferrin levels of these patients were determined.

Main Points:

- In case of preoperative anaemia of gynaecological surgery patients, treating anaemia is very important because of increased risk of postoperative morbidity and/or mortality.
- Efficacy of intravenous (IV) iron treatment in increasing maternal haemoglobin (Hb) and ferritin levels and achieving target Hb was proved in meta-analysis evaluating obstetric cases.
- In patients with iron deficiency anaemia diagnosis scheduled for elective surgery, postoperative morbidity and/or mortality risk can be decreased using IV iron treatment based on the guidelines and patient blood management strategy in the anaesthesia outpatient clinic.

Statistical analysis

The statistical analyses were performed using Statistical Package for the Social Sciences version 16.0 (SPSS Inc., Chicago, IL, USA). The data were expressed as mean±standard deviation (SD), percentage (%), or *n*, where appropriate. Differences between the preoperative and postoperative measurement parameters were presented as delta (described as mean weighted differences before and after the treatment). Statistical analysis was performed using *t*-test. A p value less than 0.05 was considered as statistically significant.

Results

Demographic data of the patients are presented in Table 1. According to the current retrospective records, the incidence of anaemia was found to be 4.23% (241/5,688), but the rate of the patients with anaemia treated with IV iron was 2.81% (160/5,688).

Moreover, 63 patients underwent gynaecological operation, and 97 underwent obstetric operation. The Hb values of the obstetric patients treated with IV iron were determined before and after the operation (10 days after the operation). The difference of values was statistically significant (delta Hb: 1.3 g dL^{-1}) (Table 2). Moreover, significant changes were observed in MCV (delta MCV: 1.9 fL), serum iron (delta serum iron: 44.4 µg dL^{-1}), serum ferritin (delta serum ferritin: 85.9 µg L^{-1}) and TIBC (delta TIBC: 211.7 µg dL^{-1}) but not in delta MCH values (Table 2).

Similarly, there was a significant change in Hb after the IV iron treatment (delta Hb: 1.25 g dL^{-1}) in patients who under-

Table 1. Demographic data (mean±SD)

	Gynaecological cases (n=63)	Obstetric cases (n=97)
Age (year)	43±7	30±5
Weight (kg)	68±5	72±3
Height (cm)	160±4	161±1

Table 2. Measurement parameters before (first measurement) and after IV iron treatment (postoperative 10th day) in the obstetric cases (mean ± SD)

Measurement parameters	First measurement	Postoperative 10th day	Difference (delta)	p
Hb (g dL^{-1})	8.9±1.1	10.3±1.1	1.3	0.000
MCV (fL)	76.2±11.3	79.1±11.2	1.9	0.000
MCH (pg)	26.1±9.8	25.7±3.4	0.3	0.012
Serum iron (µg dL^{-1})	44.7±34.1	89.1±37.8	44.4	0.008
Serum ferritin (µg L^{-1})	7.7±6.3	93.6±95.6	85.9	0.009
TIBC (µg dL^{-1})	467.8±173.1	256.1±68.9	211.7	0.001

Hb: haemoglobin; MCV: mean corpuscular volume; MCH: mean corpuscular haemoglobin; TIBC: total iron-binding capacity

Table 3. Measurement parameters before (first measurement) and after IV iron treatment (postoperative 10th day) in the gynaecological cases (mean±SD)

Measurement parameters	First measurement	Postoperative 10th day	Difference (delta)	p
Hb (g dL^{-1})	8.9±1.7	10.2±1.7	1.25*	0.000
MCV (fL)	77.6±7.7	80.4±6.2	2.2*	0.000
MCH (pg)	23.9±3.8	25.1±3.3	0.8*	0.000
Serum iron (µg dL^{-1})	29.3±64.2	163.5±121.5	133.83	0.056
Serum ferritin (µg L^{-1})	66.6±20.9	347.4±310.6	215.6*	0.002
TIBC (µg dL^{-1})	385.2±115.8	198.3±142.2	131.6*	0.077
Reticulocyte (%)	63.1±23.2	144.71±78.1	74.2	0.383
Transferrin saturation (%)	332.4±85.9	272.25±58.9	41.5	0.044

Hb: haemoglobin; MCV: mean corpuscular volume; MCH: mean corpuscular haemoglobin; TIBC: total iron-binding capacity

went gynaecological operation. When other measurement parameters were evaluated, the MCV (delta MCV: 2.2 fL), MCH (delta MCH: 0.8 pg), serum ferritin (delta serum ferritin: 215.6 µg L^{-1}) and transferrin saturations (delta transferrin saturation: 41.5%) were significant. In contrast to obstetric patients, delta serum iron, TIBC and reticulocyte count were not significant (Table 3).

Blood transfusion was required in 2 out of 97 patients underwent obstetric operation (2.06%) and 7 out of 63 patients underwent gynaecological operation (11.1%).

Discussion

The efficacy of IV iron treatment in surgical patients with preoperative IDA diagnosis in terms of Hb, MCV, MCH, serum ferritin and iron, TIBC and transferrin saturation along with reticulocyte levels has been demonstrated in this retrospective study.

Richards et al. (9) reported that the preoperative anaemia prevalence was 23.9% in 12,836 patients underwent gynaecological surgery. More blood transfusion was required in patients with preoperative anaemia than those without anaemia that resulted in an increased postoperative mortality and/or morbidity. According to our data, anaemia prevalence was 4.23% (241/5,688), but the rate of patients treated for anaemia was 2.81% (160/5,688). In 2019, anaemia prevalence in approximately 1,000 obstetric cases was found to be 9.7% in our unit.

In the literature, oral iron (iron sulphate, fumarate, ascorbate or iron polymaltose complex) was compared with IV iron (iron sucrose, FCM or low molecular iron dextran) treatment in pregnant women with IDA diagnosis during pregnancy (10-12). It has been demonstrated that target Hb level was achieved in a shorter time in many pregnant women with better social functioning when oral iron treatment was compared with IV iron (FCM) treatment in 252 pregnant women with IDA diagnosis in the 2nd or 3rd trimester (10). According to the latest meta-analysis, IV iron treatment was proved to be more efficient with less adverse effects in increasing the maternal Hb and ferritin levels as well as reaching the target Hb level (11, 12). In our study, delta value (which was mean weighted difference in Hb and ferritin before and after the treatment) was preferred similar to that in the meta-analysis. We have observed the efficacy of IV iron treatment in a 10-day-long short period in terms of increased delta Hb and delta ferritin levels.

When the records of an outpatient preoperative anaesthesia clinic were evaluated retrospectively, the anaemia prevalence was reported to be 29% in a total of 1,101 patients sched-

uled for the elective surgery, and 10.5% of them were patients who underwent gynaecological–obstetric surgery. Almost half of those patients were treated with IV FCM, and the highest increase in the Hb level was observed 22–28 days before the surgery (13). However, there was a significant 50% or greater reduction in the blood transfusion requirement in the patients who underwent gynaecological–obstetric operation treated with IV FCM than that of the patients with anaemia without treatment (13). According to the ESA guidelines on perioperative severe bleeding management in 2017 and the updated preoperative evaluation in 2018, primarily, IV iron treatment before the elective surgery along with the patient blood management (PBM) principles and goal-directed transfusion policies have been recommended because the presence of preoperative anaemia is a strong predictor that increases the need for blood transfusion in patients with IDA (7, 14). Based on this information, we conducted our study in patients who underwent gynaecological–obstetric surgery. We observed that blood transfusion was performed in 2 out of 97 patients (2.06%) who had undergone obstetric surgery and in 7 out of 63 patients (11.1%) who had undergone gynaecological surgery.

In the diagnosis of isolated IDA, the determination of serum ferritin level is very valuable because it directly indicates the iron storage. Transferrin, an iron carrier molecule, represents iron levels in the plasma, and the normal reference interval value is 12%–45% in women. In the diagnosis of isolated IDA, although the percentage of hypochromic microcytic erythrocytes is used, other markers such as reticulocyte Hb are also helpful in the diagnosis of inflammatory conditions (2). In this study, the patients with anaemia with confirmed laboratory results during the preoperative evaluation in addition to Hb concentration and reported MCV, MCH, TIBC, serum ferritin, serum iron and transferrin levels before and after IV iron treatment were recorded, and the efficacy of the treatment was evaluated. Although oral iron is the first-line option in the treatment of anaemia during pregnancy because of its dose-limiting unwanted side effects such as nausea, reflux and constipation (4), the guidelines recommend considering IV iron treatment before emergency or elective surgery.

The efficacy of single- or high-dose IV iron treatments (FCM or isomaltoside) has been shown in randomised controlled trials (15, 16). When women with postpartum haemorrhage (>1,000 mL blood loss or Hb 5.6–8.1 g dL^{-1}) were given single-dose IV of 1,500 mg isomaltoside or erythrocyte suspension, IV iron treatment resulted in increased reticulocytosis in the first week and increased Hb concentration was observed between 3 and 12 weeks (15). In a comparative study, women with IDA diagnosis having severe menstrual bleeding and Hb of 11 g dL^{-1}, more effective correction of iron stores and improved quality of life were obtained after high-dose IV FCM (each week 1,000 mg in 15 min till reaching the calculated dose) (16). In this study, a single dose of 500 mg IV iron had been preferred in obstetrics (caesarean sections).

One of the limitations of this retrospective study is the calculation of the anaemia prevalence according to the records of patients with anaemia treated with IV iron. In our hospital, PBM implementation hasstarted as a pilot study in the gynaecological and obstetric cases. Therefore, performing a thorough scanning of preoperative anaemia prospectively before the elective surgery, and subsequently, its treatment would be a more important step for PBM implementation. Another limitation is although records of Hb, MCV, MCH, TIBC, serum ferritin, iron and transferrin and reticulocyte count before and after the treatment were present in the gynaecological cases, we could obtain only complete blood count, serum ferritin and iron and TIBC in the obstetric cases because the most common anaemia type is IDA.

Conclusion

The need for blood transfusion and subsequently the postoperative morbidity and/or mortality risk can be decreased in patients with IDA diagnosis scheduled for the elective surgery by implementing preoperative IV iron treatment based on the guidelines and PBM strategy in the anaesthesia outpatient clinic.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Gazi University (Decision number 830, date 12.11.2018).

Informed Consent: Due to the retrospective design of the study, informed consent was not taken.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – D.B.G., G.I.; Design – G.I., D.B.G.; Supervision – D.B.G., Z.B., N.B., A.O.; Resources – G.I., S.B.; Materials – G.I.; Data Collection and/or Processing – G.I., S.B., G.İnan.; Analysis and/or Interpretation – D.B.G., G.I., G.İnan.; Literature Search – S.B., D.B.G., G.I., G.İnan.; Writing Manuscript – D.B.G., S.B., G.I.; Critical Review – A.O., Z.B.

Conflict of Interest: The authors have no conflicts of interest to declare.

Financial Disclosure: The authors declared that this study has received no financial support.

References

1. The Global Prevalence of Anaemia in 2011. Available from: https://apps.who.int/iris/bitstream/handle/10665/177094/9789241564960_eng.pdf?sequence=1.
2. Roy, NB, Pavord, S. The management of anaemia and haematinic deficiencies in pregnancy and post-partum. Transfusion Med 2018; 28: 107-16. [Crossref]

3. Tunkyi K, Moodley J Anemia and pregnancy outcomes: A longitidunal study. J Maternal Fetal Neonatal Med 2018; 31: 2594-8. [Crossref]
4. Breymann C. Iron Deficiency Anemia in Pregnancy. Semin Hematol 2015; 52: 339-47. [Crossref]
5. Guralnik JM, Eisenstaedt RS, Ferrucci L, Klein HG, Woodman RC. Prevalence of anemia in persons 65 years and older in the United States: evidence for a high rate of unexplained anemia. Blood 2004; 104: 2263-8. [Crossref]
6. Spahn DR, Goodnough LT. Alternatives to blood transfusion. Lancet 2013; 381: 1855-65. [Crossref]
7. Kozek-Langenecker SA, Ahmed AB, Afshari A, Albaladejo P, Aldecoa C, Barauskas G, et al. Management of severe perioperative bleeding guidelines from the European Society of Anaesthesiology First update 2016. Eur J Anaesthesiol 2017; 34: 332-95. [Crossref]
8. Muñoz M, Peña-Rosas JP, Robinson S, Milman N, Holzgreve W, Breymann C, et al. Patient blood management in obstetrics: management of anaemia and haematinic deficiencies in pregnancy and in the post-partum period: NATA consensus statement. Transfus Med 2018; 28: 22-39. [Crossref]
9. Richards T, Musallam KM, Nassif J, Ghazeeri G, Seoud M, Gurusamy KS, et al. Impact of Preoperative Anaemia and Blood Transfusion on Postoperative Outcomes in Gynaecological Surgery. PLoS One 2015; 10: e0130861. [Crossref]
10. Breymann C, Milman N, Mezzacasa A, Bernard R, Dudenhausen J; FER-ASAP investigators. Ferric carboxymaltose vs. oral iron in the treatment of pregnant women with iron deficiency anemia: an international, open-label, randomized controlled trial (FER-ASAP). J Perinat Med 2017; 45: 443-53. [Crossref]
11. Govindappagari S, Burwick RM. Treatment of iron deficiency anemia in pregnancy with intravenous versus oral iron: systematic review and meta-analysis. Am J Perinatol 2019; 36: 366-76. [Crossref]
12. Lewkowitz AK, Gupta A, Simon L, Sabol BA, Stoll C, Cooke E, et al. Intravenous compared with oral iron for the treatment of iron-deficiency anemia in pregnancy: a systematic review and meta-analysis. J Perinatol 2019; 39: 519-32. [Crossref]
13. Ellermann I, Bueckmann A, Eveslage M, Buddendick H, Latal T, Niehoff D, et al. Treating Anemia in the Preanesthesia Assessment Clinic: Results of a Retrospective Evaluation. Anesth Analg 2018; 127: 1202-10. [Crossref]
14. De Hert S, Staender S, Fritsch G, Hinkelbein J, Afshari A, Bettelli G, et al. Preoperative evaluation of adults undergoing elective noncardiac surgery: Updated guideline from the European Society of Anaesthesiology. Eur J Anaesthesiol 2018; 35: 407-65. [Crossref]
15. Holm C, Thomsen LL, Norgaard A, Langhoff-Roos J. Single-dose intravenous iron infusion or oral iron for treatment of fatigue after postpartum haemorrhage: a randomized controlled trial. Vox Sang 2017; 112: 219-28. [Crossref]
16. Van Wyck DB, Mangione A, Morrison J, Hadley PE, Jehle JA, Goodnough LT. Large-dose intravenous ferric carboxymaltose injection for iron deficiency anemia in heavy uterine bleeding: a randomized, controlled trial. Transfusion 2009; 49: 2719-28. [Crossref]