

## ORIGINAL RESEARCH ARTICLE

# Intravenous iron therapy for treating patients with iron deficiency anaemia during the perioperative period of gynecological malignancy

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## Abstract

Anaemia is a common phenomenon in patients with malignant gynecological tumors. The occurrence of anaemia in the perioperative period leads to an increased probability of blood transfusion, increased surgical complications, poor wound healing, prolonged hospitalization, increased medical costs, and increased mortality. Intravenous iron, which is known for its rapid onset and lack of gastrointestinal side effects, has become increasingly prevalent in clinical practice. A total of 300 patients with gynaecological malignancies were admitted to The First Affiliated Hospital, Hengyang Medical School, University of South China between January, 2019 and December, 2021. Anaemia was assessed during routine blood tests by measuring red blood cell (RBC) counts, hemoglobin (Hb) levels, haematocrit (HCT) values, mean corpuscular volume (MCV), and mean corpuscular hemoglobin (MCH). The postoperative blood transfusion rate, transfusion volume, infection rate, and hospitalization duration were also recorded and comparisons were made between the control and treatment groups. Our study showed that preoperative intravenous iron injection can effectively increase haemoglobin levels in patients with anemia caused by gynecological cancer, reduces the probability of perioperative blood transfusion, decreases postoperative complications and infection rates, shortens hospital stays, and improves short-term prognosis in patients. We concluded that intravenous iron presents is a valuable clinical option for addressing perioperative anaemia in patients with gynecologic malignancies. (*Afr J Reprod Health* 2024; 28 [12]: 82-87).

**Keywords:** Intravenous iron; iron deficiency anemia; gynecological malignancy

## Résumé

L'anémie est un phénomène courant chez les patientes atteintes de tumeurs gynécologiques malignes. La survenue d'une anémie pendant la période périopératoire entraîne une probabilité accrue de transfusion sanguine, une augmentation des complications chirurgicales, une mauvaise cicatrisation des plaies, une hospitalisation prolongée, une augmentation des coûts médicaux et une mortalité accrue. Le fer intraveineux, connu pour son action rapide et son absence d'effets secondaires gastro-intestinaux, est devenu de plus en plus répandu dans la pratique clinique. Au total, 300 patientes atteintes de tumeurs malignes gynécologiques ont été admises au premier hôpital affilié de la faculté de médecine de Hengyang de l'université de Chine du Sud entre janvier 2019 et décembre 2021. L'anémie a été évaluée lors d'analyses sanguines de routine en mesurant le nombre de globules rouges (GR), le taux d'hémoglobine (Hb), les valeurs d'hématocrite (HCT), le volume corpusculaire moyen (VGM) et le volume corpusculaire moyen d'hémoglobine (MCH). Le taux de transfusion sanguine postopératoire, le volume de transfusion, le taux d'infection et la durée d'hospitalisation ont également été enregistrés et des comparaisons ont été faites entre les groupes témoin et de traitement. Notre étude a montré que l'injection intraveineuse préopératoire de fer peut augmenter efficacement les taux d'hémoglobine chez les patients souffrant d'anémie causée par un cancer gynécologique, réduit la probabilité de transfusion sanguine périopératoire, diminue les complications postopératoires et les taux d'infection, raccourcit les séjours à l'hôpital et améliore le pronostic à court terme des patients. Nous avons conclu que le fer intraveineux constitue une option clinique précieuse pour traiter l'anémie périopératoire chez les patientes atteintes de tumeurs gynécologiques malignes. (*Afr J Reprod Health* 2024; 28 [12]: 82-87).

**Mots-clés:** Fer intraveineux ; anémie ferriprive; malignité gynécologique

## Introduction

Perioperative patients are prone to anaemia, with a prevalence ranging from 20% to 37% in gynaecological patients<sup>1-2</sup>. Anemia can be

categorized based on red blood cell morphology into macrocytic, normocytic, and microcytic hypochromic anemia. It can also be classified as acute or chronic, depending on its rate of progression, or by hemoglobin concentration into

mild, moderate, severe, and very severe anaemia. Another classification system distinguishes proliferative anemias, such as hemolytic, iron deficiency, and megaloblastic anemia, from hypoproliferative anemias, based on bone marrow activity<sup>3-4</sup>.

Iron deficiency anemia (IDA) occurs because of the depletion of iron stores, leading to reduced haemoglobin (Hb) synthesis and impaired red blood cell production<sup>5-6</sup>. Anaemia in patients with gynecological diseases is mostly caused by iron deficiency, which is particularly common in the perioperative period for gynecological malignant tumors, with an incidence of 81.4%<sup>7-8</sup>. IDA poses significant risks to gynecologic oncology patients, including increased mortality, complications, extended hospital stays, delayed recovery, and poorer prognosis<sup>9-11</sup>.

Treatment options for iron deficiency anemia (IDA) include blood transfusions, oral iron supplementation, and intravenous iron supplementation. Among these, intravenous iron has emerged as a key therapeutic agent for correcting anaemia owing to its rapid onset of action, absence of gastrointestinal side effects, and ability to quickly elevate haemoglobin levels. As a result, intravenous iron is increasingly recommended as a first-line treatment for IDA in patients undergoing perioperative gynecologic procedures, pregnant women, and those with chronic kidney disease<sup>12-13</sup>. This study retrospectively analyzed the efficacy of preoperative intravenous iron therapy in patients with gynecological cancer. We evaluated the changes in haematological indices before and after treatment, examined the responsiveness of different patient groups to intravenous iron therapy, and assessed the effectiveness of this therapy on intraoperative blood transfusions and short-term patient outcomes. These findings aim to inform the rational use of intravenous iron in clinical practice.

## Methods

A total of 300 patients with gynaecological malignancies admitted to The First Affiliated Hospital, Hengyang Medical School, University of South China between January, 2019 and December, 2021. Including; cervical malignancies (132 cases), endometrial cancer (64 cases), and ovarian cancer (104 cases). The eligible patients had the following characteristics: (1) patients undergoing elective

surgical intervention, (2) postoperative pathology confirming gynecologic malignancy, (3) anaemia diagnosed upon the first haematological examination upon admission, and (4) patients aged 18-75 years.

The exclusion criteria were: (1) endoscopic surgery, (2) receipt of preoperative allogeneic blood transfusions, (3) preoperative treatment for anaemia with oral iron, folic acid, vitamin B12, or erythropoietin, (4) discontinuation of treatment due to adverse reactions, and (5) concurrent liver or kidney impairment.

## Methods of treatment

On the first day of hospitalization, all patients underwent haematological investigations and were randomly assigned to either the treatment or control group based on whether they received intravenous iron therapy. The control group received preoperative routine fluid rehydration and nursing from the second day of admission, whereas the treatment group received intravenous iron supplementation in addition to routine fluid rehydration and nursing. The intravenous iron regimen for the treatment group consisted of Iron Sucrose Injection (Veloflor) at 300 mg IV. The first dose was administered slowly by titrating 25 mg over at least 15 minutes, followed by titration of the remaining dose over 30 minutes, provided no adverse reactions occurred. The treatment duration ranged from 3 to 5 days, depending on the individual iron supplementation requirements of each patient. Blood tests were repeated on the morning of surgery. The median interval from the start of treatment to the day of surgery was 6 days (approximately 4-8 days). Haematological indicators were obtained from peripheral venous blood samples collected in the fasting state on the day of surgery. All surgeries were performed by senior surgeons, and the pathology specimens were reviewed by two senior pathologists in the hospital.

## Observation indicators

Anaemia was assessed during routine blood tests by measuring red blood cell (RBC) counts, hemoglobin (Hb) levels, and haematocrit (HCT) values, mean corpuscular volume (MCV), and mean corpuscular hemoglobin (MCH). The postoperative blood transfusion rate, transfusion volume, infection rate, and hospitalization duration were also recorded and comparisons were made between the control and

treatment groups. All patients were followed up for 3 to 6 months postoperatively, and repeat blood tests were conducted after two weeks and one month of surgery.

### **Statistical analysis**

SPSS 26.0 version was used for statistical analysis. The mean±standard deviation (SD) was used to represent the data that followed a normal distribution. Comparisons between the two groups were performed using a T-test, while one-way ANOVA was employed for comparisons across multiple groups. In the treatment group, a t-test was used to compare hematological indices before and after treatment. Similarly, a t-test was conducted to compare hematological indices between the treatment and control groups.

### **Ethical considerations**

This study was approved by the Ethics Committee of the First Affiliated Hospital of the University of South China (No. 2023LL1120001, 20/11/2023). All the participants signed an informed consent form.

## **Results**

### **Comparison of hematological test or nutritional indexes after treatment**

There were significant differences in haematological indices (RBC, Hb, HCT, MCV, and MCH) between the control groups and after intravenous iron treatment groups ( $P < 0.001$ , Table 1, Figure 1). However, there were no significant differences in postoperative MCHC, total protein or serum albumin levels ( $P > 0.05$ , Table 1, Figure 2).

### **Comparison of short-term prognosis between intravenous iron treatment and control groups**

The overall intraoperative blood transfusion rate was 22% (66/300). The rate of blood transfusion was higher in the control group than in the treatment group (30.6% vs. 13.2%,  $P = 0.002$ ). Postoperative complications occurred in 31% of the patients (93/300). The incidence of complication rate in the treatment group was much lower than that in the control group (20.9% vs. 44.5%,  $P = 0.008$ ). Compared with the control group, postoperative

hospitalization days were shorter in the treatment group ( $10.69 \pm 3.18$  days) than in the control group ( $12.86 \pm 3.72$  days,  $P < 0.001$ , Table 2, Figure 3).

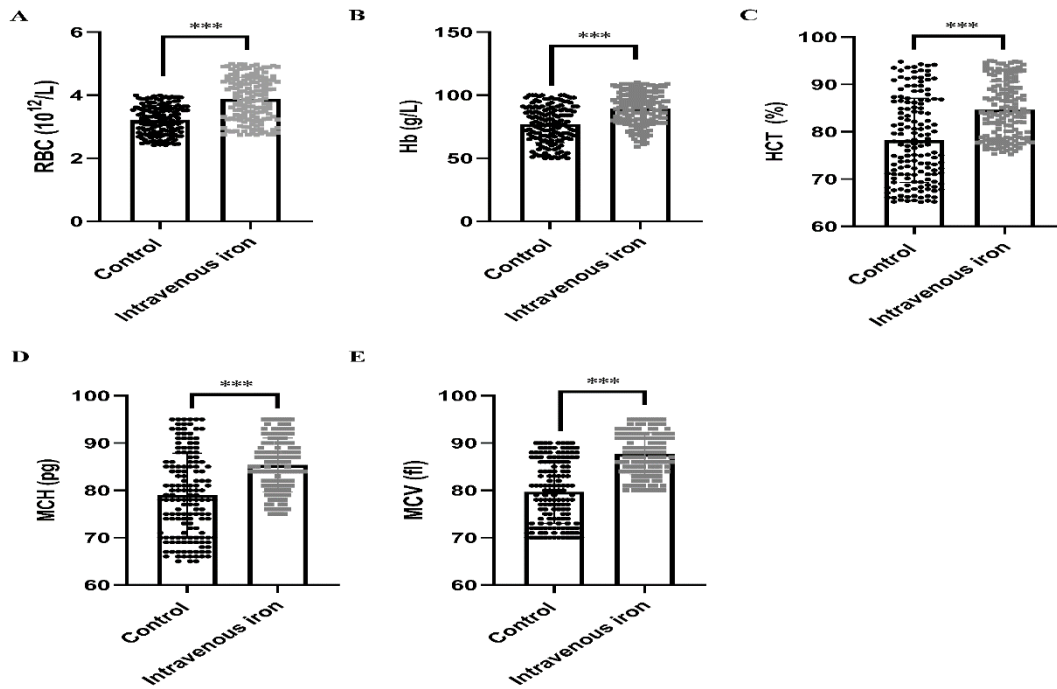
## **Discussion**

Anaemia is prevalent in gynaecological malignancies and other gynaecological diseases, owing to both the nature of the disease and the surgical procedures involved<sup>14-15</sup>. Statistics indicate that perioperative anaemia in gynaecologic tumours has several negative impacts, including an increased likelihood of blood transfusions, higher 30-day postoperative mortality, and a significantly higher incidence of complications such as cardiac, respiratory, central nervous system issues, and sepsis<sup>16-17</sup>. Additionally, anaemia heightens the risk of perioperative complications, extends hospital stays, and is associated with poorer prognosis in malignancies<sup>18-19</sup>. Thus, it is crucial to address anaemia in patients with gynaecological tumours by implementing effective measures to correct anaemia before surgery to enhance postoperative recovery. Intravenous iron therapy is a common intervention for gynaecological anaemia, and retrospective cohort studies have demonstrated its efficacy in significantly increasing haemoglobin levels in patients with tumor-associated anaemia<sup>20-21</sup>. This study revealed that the preoperative administration of intravenous iron in patients with gynaecological malignancy-related anaemia effectively improved haemoglobin levels, reduced the probability of perioperative blood transfusion and the probability of postoperative complications, shortened postoperative hospitalization days, and improved short-term outcomes. Therefore, timely correction of perioperative anaemia in patients with gynaecological tumours is of significant therapeutic importance.

This study confirmed that perioperative iron deficiency anemia patients with gynecologic malignant tumors affect postoperative recovery, which provides a theoretical basis for early iron supplementation and improvement of prognosis in perioperative iron deficiency and iron deficiency anemia patients with gynecologic malignant tumors, as well as guidance for clinical work. However, this study had some limitations. First, the study sample was mainly based on tertiary hospitals, which may have some errors in data representativeness.

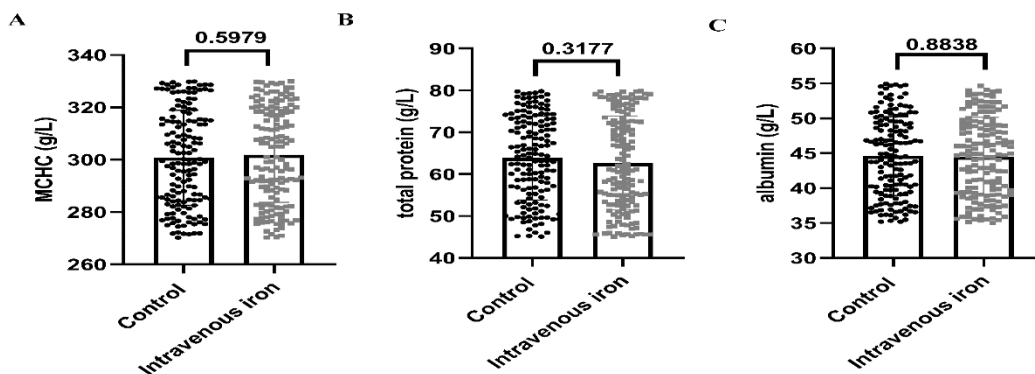
**Table 1 :** Comparison of hematological test or nutritional indexes after treatment

	Control (n=150)	intravenous iron treatment (n=150)	t value	P value
RBC ( $10^{12}/L$ )	3.2±0.5	3.9±0.7	9.9	<0.001
Hb (g/L)	76.9±14.6	89.4±13.1	7.8	<0.001
HCT(%)	78.2±8.9	84.7±6.0	7.4	<0.001
MCV(fl)	79.7±6.6	87.7±4.4	12.3	<0.001
MCH(pg)	79.0±8.8	85.4±5.7	7.4	<0.001
MCHC(g/L)	300.8±18.2	301.9±18.0	0.5	0.6
Total protein	63.9±10.0	62.7±11.2	1.0	0.3
Albumin	44.6±5.7	44.5±5.6	0.1	0.9



A-E There were significant differences in hematological indexes (RBC, Hb, HCT, MCV, MCH) between the control groups and after intravenous iron treatment groups

**Figure 1:** Comparison of hematological test indexes after intravenous iron treatment

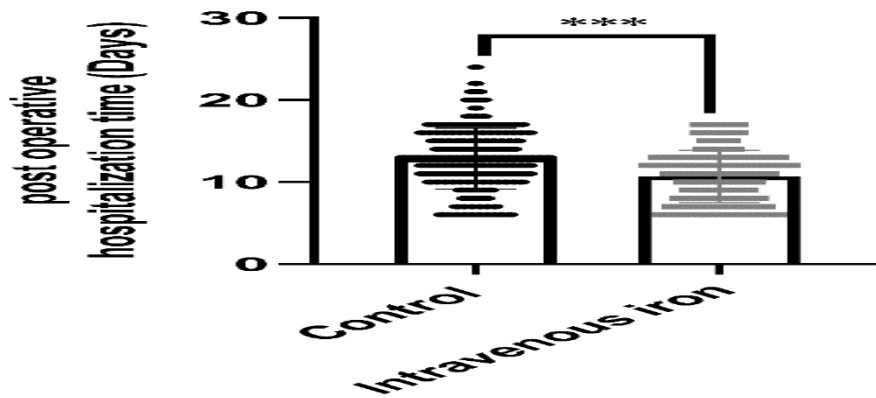


A-C Postoperative levels of MCHC, total protein, and albumin did not show significant differences between the control groups and after intravenous iron treatment groups

**Figure 2:** Comparison of nutritional indexes after intravenous iron treatment

**Table 2:** Intraoperative blood transfusion, postoperative hospital stay, and postoperative complications in two groups of patients

		Control (n=150)	intravenous iron treatment (n=150)	$\chi^2$ value	P value
Intraoperative blood transfusion	with	46	20	13.1	0.002
	without	104	130		
postoperative complications	with	67	45	7.0	0.008
	without	83	105		
postoperative hospital stay		12.9±3.7	10.7±3.2	5.3	<0.001



**Figure 3:** Intravenous iron reduces the probability of blood transfusions and associated risks but also shortens hospital stays and lowers postoperative complications

Nextly, this study did not compare the impact on postoperative recovery in patients treated with different intravenous iron agents.

In conclusion, intravenous iron supplementation is safe and effective in the treatment of perioperative anemia in women. It not only reduces the probability of blood transfusions and associated risks but also shortens hospital stays and lowers postoperative complications. Furthermore, intravenous iron significantly increased hemoglobin levels while minimizing gastrointestinal side effects. Therefore, intravenous iron injection is an important choice for the treatment of gynecological tumors in patients with perioperative anemia and has important clinical significance.

**Conflicting interests**

The authors declare that they have no conflicts of interest.

**Ethical consideration**

All experiments performed in studies involving human participants were approved by the Ethics

Committee of The First Affiliated Hospital, University of South China(Grant No. 2023LL1120001).

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**Authors’ contributions**

ZZD and JMZ conceptualised this study. ZZD, XZ, GCH, NY, and JMZ worked on the literature review. ZZD, XZ, and JMZ worked on the data analysis and interpretation of results. All authors worked on the discussed of the findings. The final manuscript had been read and approved by all the authors.

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