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Original Research Article

Clinical efficacy of polysaccharide iron complex plus vitamin C in the treatment of iron deficiency anemia in pregnancy and their effect on iron metabolism

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Abstract

Purpose: *To evaluate the clinical efficacy of polysaccharide iron complexes (PIC) plus vitamin C in treating iron deficiency anemia (IDA) during pregnancy and its effect on iron metabolism.*
Methods: *Ninety pregnant women with IDA in their second trimester admitted into the Department of Gynaecology and Obstetrics, Nanchang Third Hospital, Jiangxi Province, China between June 2019 and June 2021 were randomly and equally assigned to receive either PIC (two 500 mg capsules daily) alone (control group) or PIC plus vitamin C (0.1 g daily) (study group) for 4 weeks. Efficacy was determined by changes in clinical symptoms and blood indices and iron metabolism indices (serum ferritin, serum iron, hepcidin, transferrin saturation) pre- and post-treatment. Adverse pregnancy outcomes were also recorded.*
Results: *Both groups were comparable at baseline. Post-treatment, study group showed significantly higher red blood cell (RBC), hemoglobin (Hb), mean red blood cell volume (MCV) and mean corpuscular hemoglobin (MCH) compared to control group ($p < 0.05$). Iron metabolism indices also significantly improved in study group with serum ferritin (SF), serum iron (SI), hepcidin (Hepc), and transferrin saturation (TSAT) ($p < 0.05$). The total clinical efficacy was higher in study group ($p < 0.05$), and the incidence of adverse pregnancy outcomes was lower ($p < 0.05$).*
Conclusions: *The combination of PIC with vitamin C significantly improves the hematological indices, enhances iron metabolism, and reduces adverse pregnancy outcomes compared to PIC alone in pregnant women with IDA. Further studies with larger sample sizes are warranted to validate these results.*

Keywords: *Polysaccharide iron complex, Vitamin C, Iron deficiency anemia, Pregnancy, Iron metabolism*

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INTRODUCTION

Iron deficiency anemia is a prevalent condition among pregnant women, with its occurrence estimated at 26.03 % in China. This condition, characterized by the insufficient presence of iron in the body, have significant implications during pregnancy. It leads to diminished immune

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function and reduced tolerance to the physiological stresses of surgery and delivery. These alterations are linked to several adverse outcomes, such as increased blood pressure, fatigue, dizziness, nausea, and loss of appetite. Additionally, the increase in blood volume typical during pregnancy exacerbate these effects. These factors collectively contribute to an elevated risk of complications such as miscarriage, preterm birth, and low birth weight in newborns. Therefore, effective management of patients with iron deficiency anemia during pregnancy is essential in protecting maternal and infant health and improving prognosis [1,2].

The treatment of iron deficiency anemia in pregnancy is mainly performed by oral administration of iron agents, intravenous injections of iron preparations, and blood transfusions. However, the treatment efficacy is inconsistent [3]. Polysaccharide iron complex is an iron supplement, a common clinical anti-anemia drug, that contains 46 % elemental iron which is non-irritating to the gastric mucosa and provides a marked improvement in serum iron concentrations [4]. Vitamin C is a vitamin supplement necessary for the maintenance of body functions, with cellular tissue repair and antioxidant effects. Proper vitamin C supplementation enables the reduction of difficult-to-absorb trivalent iron to easy-to-absorb divalent iron and promotes the reduction of folic acid to tetrahydrofolate, which aids in the prevention and treatment of iron deficiency anemia as well as megaloblastic anemia [5].

High concentrations of vitamin C facilitate the reduction of amino acids in proteins to cysteine, boost antibody synthesis, and enhance body immunity [6]. Evidence has revealed significant therapeutic benefits of combining polysaccharide iron complex with vitamin C such as normalization of plasma iron concentrations in pregnant women, enhancement of physiological indices, and obviation of adverse pregnancy outcomes [7]. The current study was performed to investigate the clinical efficacy of polysaccharide iron complex combined with vitamin C in the treatment of iron deficiency anemia in pregnancy and their effect on iron metabolism.

METHODS

Participants

Ninety pregnant women experiencing iron deficiency anemia, specifically in their second trimester, were admitted to the Department of Gynaecology and Obstetrics, Nanchang Third Hospital, Nanchang City, Jiangxi Province, China between June 2019 and June 2021. These patients were randomly allocated using a number table method into two groups: control group received polysaccharide iron complex and study group received polysaccharide iron complex plus vitamin C, with each group comprising 45 individuals. This study's procedures strictly followed the ethical standards set by the Declaration of Helsinki's clinical research guidelines, updated in 2023 [7]. The research obtained authorization from the Nanchang Third Hospital Ethics Committee (approval no. EC/NTH/2023/0524).

Inclusion and exclusion criteria

Patients who met the relevant clinical diagnostic criteria for iron deficiency anemia in pregnancy with diagnosis confirmed by relevant pathological examination, patients with singleton pregnancies, patients and fetuses with stable vital signs and patients without mental illness and disorders of consciousness were included in the study.

Patients who had other serious pregnancy comorbidities, mental disorders that prevented cooperation in completing the study, patients with fetal abnormalities in prenatal diagnosis and those with incomplete data were excluded from the study.

Treatments

In control group, patients were instructed to consume more iron-rich foods such as animal liver, soy products, eggs, green leafy vegetables, seaweed and lean meat in their daily diet. They were administered two polysaccharide iron complex capsules, each containing 500 mg of iron (Shanghai Pharmaceutical Group Qingdao Guofeng Pharmaceutical Co., Ltd., Lot no. 170709) once daily via the oral route.

Patients in study group received polysaccharide iron complex capsules (same as control group) and 0.1 g of oral vitamin C (Shaanxi Yishengtang Pharmaceutical Co., Ltd., product lot no. 20190423) once daily orally. Treatment duration was for 4 consecutive weeks in both groups.

Evaluation of parameters/indices

Blood test indices

Venous blood samples (5 mL) were obtained from patients pre- and post-treatment over 4 weeks. These samples were analyzed to measure red blood cell count (RBC), hemoglobin (Hb), mean red blood cell volume (MCV), and

mean corpuscular hemoglobin (MCH) levels in both cohorts. The analyses were conducted using the DxH800 automatic hematocrit analyzer by Beckman Coulter, USA.

Clinical efficacy

Clinical efficacy is said to be *Markedly effective* (ME) when clinical symptoms such as dizziness and fatigue disappear, RBC count is > 3.5 × 10^{12}/L and Hb content is ≥ 100 g/L. It is *Effective* (E) when clinical symptoms such as dizziness and fatigue are significantly mitigated, RBC is higher than before treatment and Hb content is ≥ 20 g/L. it is *ineffective* (IE) when there is no improvement or there is an aggravation of clinical symptoms, no significant change in RBC count and an increase in Hb level of < 20 g/L. Total clinical efficacy (TC) was calculated using Eq 1.

TC (%) = {(ME+E)/TN}100 …….. (1)

Where TN is the total number of cases.

Iron metabolism indices

Venous blood samples were taken from fasting patients both before the initiation and after 4 weeks of treatment. The serum was isolated, and levels of serum ferritin (SF), serum iron (SI), hepcidin (Hepc), and transferrin saturation (TSAT) were quantified using enzyme-linked immunosorbent assays. Adherence to kit's instruction was rigorously maintained during assay procedures to guarantee the precision of test outcomes.

Adverse pregnancy outcomes

Adverse pregnancy outcomes were recorded, which included maternal postpartum complications (puerperal infection, premature rupture of membranes, postpartum hemorrhage, hyperemesis) and adverse perinatal outcomes (preterm birth, fetal distress, and low birth weight infants).

Statistical analysis

Data management and analysis were conducted using SPSS 26.0 statistical software. Measured data are presented as mean ± standard deviation (SD) and were analyzed using *t*-test. Count data are represented as percentages (%) and evaluated using chi-square test. A *p*-value of less than 0.05 was deemed to indicate statistical significance.

RESULTS

Baseline clinical profiles

Control group, comprised 23 primipara and 22 multipara, the age range was 22 - 36 years (mean 26.35 ± 2.27), with gestational weeks ranging from 17 to 35 (mean 25.14 ± 3.36). Anemia classification was based on hemoglobin levels: 18 cases were identified as mild anemia (Hb 10.0 - 10.9 g/dL for the first and third trimesters, and Hb 10.0 - 11.0 g/dL for the second trimester), 21 cases as moderate anemia (Hb 7.0 - 9.9 g/dL), and 6 cases as severe anemia (Hb < 7.0 g/dL). In study group, there were 25 primipara and 20 multipara, aged 23 - 35 years (mean 25.42 ± 2.38), with gestational weeks of 16 - 36 (mean 26.16 ± 3.22). This group had 15 cases of mild anemia, 23 of moderate anemia, and 7 of severe anemia, classified using the same hemoglobin criteria. Baseline clinical profiles between the two groups showed no significant differences ($p > 0.05$; Table 1).

Clinical efficacy

Polysaccharide iron complex was associated with higher treatment efficacy when co-administered with vitamin C versus when administered alone ($p < 0.05$; Table 2).

Table 1: Baseline clinical profiles (n=45)

Parameter	Study	Control	t/x²	*P*-value
Pregnant women			0.179	0.673
Primipara	23	25	-	-
Multipara	22	20	-	-
Age (years)	22-36	23-35	-	-
Mean age (years)	26.35±2.27	25.42±2.38	1.897	0.061
Gestation (weeks)	17-35	16-36	-	-
Mean gestation (weeks)	25.14±3.36	26.16±3.22	1.47	0.145
Degree of anemia				
Mild anemia	18	15	0.351	0.554
Moderate anemia	21	23	0.01	0.920
Severe anemia	6	7	0.263	0.608

Table 2: Clinical efficacy (n=45)

Group	Markedly effective	Effective	Ineffective	Total efficiency
Study	27	15	3	42(93.33)*
Control	21	14	10	35(77.78)
x^2	-	-	-	4.406
P-value		-	-	0.036

*$P < 0.05$ vs. control.

Table 3: Blood test indices (n=45)

Blood test indices		Study	Control	T	*P*-value
RBC ($\times 10^{12}$/L)	Before treatment	2.20±0.41	2.07±0.38	1.56	0.122
	After treatment	5.03±0.36*	3.67±0.29	19.735	<0.001
Hb (g/L)	Before treatment	83.68±3.26	82.77±3.29	1.318	0.191
	After treatment	117.37±3.43*	101.28±3.23	22.909	<0.001
MCV (fl)	Before treatment	67.84±7.66	66.87±7.48	0.608	0.545
	After treatment	94.36±7.54*	88.42±8.02	3.620	<0.001
MCH (pg)	Before treatment	23.37±2.25	22.46±2.29	1.901	0.061
	After treatment	32.47±2.44*	26.98±1.47	12.928	<0.001

*$P < 0.001$ vs. control; RBC: Red blood cells; HB: Haemoglobin; MCV: mean red blood cell volume; MCH: mean corpuscular hemoglobin

Table 4: Iron metabolism indices (n=45)

Iron metabolism index		Study	Control	t	*P*-value
SF (μg/L)	Before treatment	8.48±1.36	8.49±1.34	0.035	0.972
	After treatment	48.44±5.57*	31.62±8.43	11.167	<0.001
SI (μmol/L)	Before treatment	4.53±0.17	4.60±0.15	1.184	0.240
	After treatment	8.80±0.29*	6.54±0.23	40.959	<0.001
Hepc (μg/L)	Before treatment	12.39±1.45	12.51±1.51	0.385	0.701
	After treatment	36.13±3.96*	26.86±3.77	11.373	<0.001
TSAT (%)	Before treatment	18.56±2.78	18.59±2.85	0.051	0.959
	After treatment	32.14±5.87*	25.64±5.59	5.379	<0.001

*$P < 0.001$ vs. control; SF: serum ferritin; SI: serum iron; Hepc: hepcidin; TSAT: transferrin saturation

Table 5: Adverse pregnancy outcomes

Group	PI	PRM	PPH	HD	PTD	FD	LBWI	Incidence
Study	0	1	0	0	1	0	1	3(6.67)*
Control	1	2	1	1	2	1	2	10(22.22)
x^2	-	-	-	-	-	-	-	4.406
P-value	-	-	-	-	-	-	-	0.036

*$P < 0.05$ vs. control; n = 45 per group; PI: Puerperal infection; PRM: Premature rupture of membranes; PPH: Postpartum hemorrhage; HD: Hypertensive disorder; PTD: Preterm delivery; FD: Fetal distress; LBWI: Low birth weight infant

Blood test indices

Polysaccharide iron complex plus vitamin C resulted in significantly higher levels of RBC, Hb, MCV, and MCH than polysaccharide iron complex when given alone, indicating more therapeutic enrichment in blood indices of patients on combination therapy ($p < 0.05$; Table 3).

Iron metabolism indices

Superior iron metabolism was observed in the patients treated with polysaccharide iron complex in combination with vitamin C versus those given polysaccharide iron complex only, as evidenced by the significantly higher plasma concentrations of SF, SI, Hepc, and TSAT ($p < 0.05$; Table 4).

Adverse pregnancy outcomes

Polysaccharide iron complex plus vitamin C provided better mitigation on the adverse pregnancy outcomes than polysaccharide iron complex alone ($p < 0.05$; Table 5).

DISCUSSION

Iron deficiency anemia, characterized as the most common form of small-cell hypochromic anemia, is particularly prevalent among pregnant

women. This high prevalence is due to significant physiological changes during pregnancy that affect iron metabolism. These changes include alterations in immunity and the body's ability to regulate iron absorption and excretion effectively. Key predisposing factors or risk factors contributing to iron deficiency anemia in pregnancy include increased iron requirements due to the growing fetus and placenta, dilutional anemia from expanded plasma volume, and potential dietary insufficiencies. Women with heavy menstrual bleeding, a history of anemia before pregnancy, or multiple pregnancies are at higher risk. Additionally, inadequate dietary intake of iron-rich foods, certain chronic conditions like celiac disease that affect iron absorption, and gastrointestinal losses due to conditions like gastritis or helminth infections further exacerbate the risk of developing iron deficiency anemia during pregnancy [8]. Inadequate iron content in the body results in the inadequate synthesis of hemoglobin and the impaired capacity of the red blood cells to transport oxygen, which eventually causes iron deficiency anemia [9].

The development of iron deficiency anemia during pregnancy is trichotomized into three stages; firstly, in the early stage of iron deficiency anemia during pregnancy, despite a mild decrease in iron storage, the concentrations of serum ferritin, hemoglobin, and red blood cells remain in the normal range, resulting in unnoticeable symptoms [10]. Secondly, with continuous decrease of iron content, significant decline of erythropoiesis brings out more and more obvious signs and symptoms of anemia in pregnant women, with typical clinical symptoms such as pallor, weakness, easy fatigue, dizziness, shortness of breath, and abnormal nails (pale, thin and flat nails) [11]. Finally, following severe iron deficiency, hematopoietic functions of bone marrow of pregnant women is hampered, resulting in shrunken red blood cell volume and severely reduced hemoglobin amount, characterized by clinical concomitant symptoms such as abdominal pain and diarrhea [12]. Prolonged persistence of severe iron deficiency anemia in pregnancy is associated with postpartum complications (e.g., puerperal infections, postpartum hemorrhage, perineal pain, breast problems, and postpartum depression.) and adverse perinatal outcomes (preterm birth, fetal distress and low birth weight) [13].

Clinical interventions include oral and parenteral iron agents (by intramuscular or intravenous drip). Given the special physical condition of pregnant women, there is an urgent clinical need to identify better treatment options to reduce the symptoms of anemia and potential fetal dysplasia and further improve the treatment prognosis.

Polysaccharide iron complex is a low molecular weight polysaccharide iron compound that facilitates the increase of blood iron levels and hemoglobin [14]. After administration, the polysaccharide iron complex molecule regulates the blood concentration of iron through the absorption valve of the intestinal mucosa, and iron toxicity and gastrointestinal irritation or constipation have been rarely reported with its use [15]. Considering the long treatment course of the polysaccharide iron complex, it is frequently adopted in combination with other agents to optimize the intervention efficiency and enhance pregnancy outcomes [16]. Serum ferritin indicates the amount of iron in the body, and a low level indicates possible iron deficiency anemia, excessive blood loss, and iron absorption disorders. Serum iron mainly describes the amount of iron bound to transferrin in the body, and its variations identify the type and severity of anemia. MCV and MCH effectively indicate the anemia status of the body. Red blood cells are the main cells for transporting oxygen and carbon dioxide in the body and have certain immune functions. Hemoglobin transports oxygen to organs and tissues and reflect the body's ability to produce red blood cells, while Hepc and TSAT effectively reflect the iron content and its transport status in the body. In the present study, superior therapeutic enrichment in blood indices and iron metabolism was observed in the patients intervened with polysaccharide iron complex plus vitamin C versus those given polysaccharide iron complex only, as evinced by the significantly higher plasma concentrations of RBC, Hb, MCV, MCH, SF, SI, Hepc, and TSAT ($p < 0.05$). Polysaccharide iron complex plus vitamin C provided higher treatment efficacy and better mitigation of adverse pregnancy outcomes than polysaccharide iron complex alone ($p < 0.05$). The results demonstrated that the joint use of polysaccharide iron complex and vitamin C regulates iron metabolism, facilitates blood indices recovery, potentiates treatment efficiency and features a high safety profile [17]. The reason for this is that the polysaccharide iron complex is absorbed into the patient's gastrointestinal tract in the form of intact molecules after oral administration and act rapidly to increase the iron content and hemoglobin level in the blood [18]. The vast majority of dietary iron intake (80 %, as indicated by a previous study) is non-ferritin [22], which is non-absorbable by the duodenum. Vitamin C, as a strong reducing agent, complex with trivalent

iron ions in ferritin to unstable ferrous ascorbate and use its solubility to promote the absorption of non-hemoglobin in the duodenum and proximal jejunum, thus better relieving the symptoms of iron deficiency anemia [19]. Furthermore, the use of polysaccharide iron complex supplementation with vitamin C also protects the divalent iron in the polysaccharide iron complex from oxidation to trivalent iron, which increases the absorption and utilization of iron and favors the improvement of the ability of erythrocytes to transport oxygen in the body and protects maternal and infant health. It is consistent with the findings of Wang, and Li *et al* [20,21].

Limitations of this study

Limited sample size of this study introduces a potential bias risk. Future research, incorporating more robust methodologies and larger sample sizes, is essential to corroborate these findings. Such research would provide a firmer foundation for selecting treatment strategies for pregnant patients with iron deficiency anemia.

CONCLUSION

Polysaccharide iron complex plus vitamin C offers a marked symptom alleviation for patients with iron deficiency anemia in pregnancy, enhances iron metabolism, and possesses a high safety profile. Further studies with larger sample sizes are required to validate these results.

DECLARATIONS

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Ethical approval

None provided.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Conflict of Interest

No conflict of interest associated with this work.

Contribution of Authors

The authors declare that this work was done by the authors named in this article and all liabilities pertaining to claims relating to the content of this article will be borne by them.

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