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Intravenous iron isomaltoside versus oral iron supplementation in women with postpartum anaemia

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Objectives: To compare oral iron supplementation with intravenous (IV) iron isomaltoside (Monofer) in terms of haemoglobin (Hb) level, ferritin level, and fatigue at 2 and 6 weeks in women with severe postpartum anaemia.
Methods: Medical records of patients with severe postpartum anaemia (Hb ≤8 g/dL), irrespective of mode of delivery, who were admitted between January 2023 and December 2024 at Kwong Wah Hospital were retrospectively reviewed. Patients received either a single 500 mg dose of IV Monofer or oral iron supplementation, and then both groups were prescribed oral iron supplements for 12 weeks if the Hb level was ≤8.0 g/dL at discharge. Primary outcome measures included changes in Hb and ferritin levels, as well as change in Multidimensional Fatigue Inventory scores, from baseline to weeks 2 and 6. Secondary outcome measures included adverse reaction rates and changes in blood transfusion rates after implementation of the new IV Monofer protocol for severe postpartum anaemia.
Results: In total, 177 patients who received either IV Monofer (n=141) or oral iron supplementation (n=36) were included in the analysis. Compared with the oral iron group, the IV Monofer group showed greater increases in mean Hb levels at week 2 (3.11 vs 2.37 g/dL, p<0.001) and week 6 (4.89 vs 3.55 g/dL, p<0.001), as well as higher mean ferritin levels at week 2 (599.5 vs 109 pmol/L, p<0.001) and week 6 (189 vs 100 pmol/L, p<0.001). No patients experienced serious adverse reactions or anaphylaxis following IV Monofer administration. Only two (1.1%) patients reported mild adverse reactions, which resolved spontaneously.
Conclusion: A single fixed dose of IV iron isomaltoside (Monofer) resulted in more rapid improvements in Hb levels and iron stores in women with severe postpartum anaemia, compared with oral iron. IV Monofer is an effective alternative to blood transfusion for the management of severe postpartum anaemia.

Keywords: Anemia, iron-deficiency; Iron isomaltoside 1000; Postpartum hemorrhage

Introduction

Postpartum anaemia affects up to 50% of women, regardless of mode of delivery, even in well-developed countries[1]. It has become a major maternal health concern worldwide. Iron deficiency resulting from antenatal anaemia or intrapartum blood loss remains the primary cause[2]. Postpartum anaemia is associated with maternal morbidities, including postpartum depression, fatigue, and impaired cognition, which negatively affect maternal-infant bonding and quality of life[1,3]. Early iron supplementation can significantly improve health-related quality of life and reduce the risk of postpartum depression[2].

Oral iron supplementation has been the first-line treatment for women with mild to moderate postpartum iron deficiency anaemia because of its affordability and availability. However, oral supplementation takes time to have an effect and is often poorly tolerated due to adverse gastrointestinal effects, such as nausea, vomiting, and constipation, which lead to poor adherence and treatment failure. Intravenous (IV) iron acts more rapidly, is better tolerated than oral iron, and can replace blood transfusion for women with severe postpartum anaemia who have minimal symptoms or cannot tolerate or have failed oral iron therapy[4-7].

IV iron is widely used to treat severe iron deficiency anaemia in medical and gynaecological patients[8]. Compared with oral iron, it leads to more rapid improvements in haemoglobin (Hb) concentration and iron stores, making it an alternative to blood transfusion in haemodynamically stable patients with severe postpartum anaemia. In postpartum women with anaemia, IV iron isomaltoside (Monofer) has demonstrated excellent efficacy and safety[9]. Nonetheless, the absence of a control group (oral iron alone) limits direct comparison, and the dosage of IV Monofer has varied according to patients' body weight (500 mg for <50 kg

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and 1000 mg for ≥50 kg). Since 2021, our department has implemented a new protocol to treat postpartum anaemia with a standardised single dose of IV Monofer. This study aimed to compare oral iron supplementation with IV Monofer in terms of Hb level, ferritin level, and fatigue at 2 and 6 weeks in women with severe postpartum anaemia.

Methods

Medical records of patients with severe postpartum anaemia (Hb ≤8 g/dL), irrespective of mode of delivery, who were admitted between January 2023 and December 2024 at Kwong Wah Hospital were retrospectively reviewed via the Clinical Data Analysis and Reporting System. Patients who were lost to follow-up or who received blood transfusion after oral or IV iron therapy were excluded, but those who received blood transfusions prior to oral or IV iron therapy were included; their post-transfusion Hb levels were regarded as baseline values.

Complete blood count was routinely assessed on day 2 post-delivery. According to our departmental protocol, patients with postpartum haemorrhage (Hb 6-8 g/dL) or a prenatal-to-postnatal Hb drop of ≥3 g/dL were offered IV Monofer. Haemodynamically stable patients with minimal symptoms were offered either IV Monofer or oral iron supplementation, whereas patients with Hb <6 g/dL, haemodynamic instability, or severe symptoms were offered blood transfusion. In patients with Hb ≤8.0 g/dL at discharge, oral iron supplements, either ferrous sulphate 300 mg/day or iron (III) hydroxide polymaltose complex chewable tablets 100 mg/day (for those intolerant to ferrous sulphate), were prescribed for 12 weeks.

A standardised single dose of 500 mg IV Monofer infusion over 60 minutes was administered, irrespective of body weight. Vital signs, including blood pressure, pulse, temperature, and oxygen saturation, were monitored at the start of administration, every 15 minutes during infusion, at the end of infusion, and 30 minutes post-infusion. For patients with asthma or multiple drug allergies, a single dose of IV hydrocortisone 200 mg was administered prior to IV Monofer. Any adverse or hypersensitivity reactions were documented and managed accordingly.

Primary outcome measures included changes in Hb and ferritin levels, as well as change in Multidimensional Fatigue Inventory (MFI) scores, from baseline to weeks 2 and 6. Secondary outcome measures included adverse reaction rates and changes in blood transfusion rates after implementation of the new IV Monofer protocol for severe postpartum anaemia.

The self-report MFI comprises 20 items designed to evaluate fatigue[10]. Each item is rated on a five-point Likert scale ranging from 1 (yes, that is true) to 5 (no, that is not true). Total scores range from 20 to 100; higher scores indicate greater fatigue severity. The MFI has been validated across diverse populations, including individuals with anaemia as well as pregnant and postpartum women, demonstrating consistency and sensitivity[11,12]. The Hong Kong Chinese version of the MFI has also been validated[13].

Statistical analysis was performed using SPSS (Windows version 27.0; IBM Corp, Armonk [NY], United States). A p value of <0.05 was considered statistically significant. The IV Monofer group and the oral iron group were compared using the independent *t* test or Mann-Whitney *U* test for continuous variables and the Chi-squared test for categorical variables.

Results

Of 263 patients with severe postpartum anaemia (Hb ≤8 g/dL) identified, 42 were lost to follow-up, 44 received blood transfusion alone or after oral or IV iron therapy, and the remaining 177 patients who received either IV Monofer (n=141) or oral iron supplementation (n=36) were included in the analysis (Table).

The two groups were comparable in terms of maternal age, parity, mode of delivery, ethnicity, and body mass index. Most patients were Chinese, nulliparous, had spontaneous vaginal deliveries, and experienced minor postpartum haemorrhage. Thirty (16.9%) women received blood transfusion prior to oral or IV iron therapy.

Compared with the oral iron group, the IV Monofer group showed greater increases in mean Hb levels at week 2 (3.11 vs 2.37 g/dL, p<0.001) and week 6 (4.89 vs 3.55 g/dL, p<0.001), as well as higher mean ferritin levels at week 2 (599.5 vs 109 pmol/L, p<0.001) and week 6 (189 vs 100 pmol/L, p<0.001) [Table]. Post-treatment MFI scores did not significantly differ between the two groups.

In our obstetric unit, the blood transfusion rate decreased from 1.83% during 2018-2019 to 1.06% during 2023-2024 (p<0.001) following implementation of the new IV Monofer protocol for severe postpartum anaemia. Data from 2020 to 2022 were excluded due to the influence of COVID-19 pandemic on rates of postpartum haemorrhage and blood transfusions.

No patients experienced serious adverse reactions or anaphylaxis following IV Monofer administration.

Table. Characteristics and outcomes of patients with severe postpartum anaemia receiving intravenous (IV) Monofer or oral iron, followed by 12 weeks of oral iron supplementation.

Variable	IV Monofer (n=141)	Oral iron (n=36)	p Value
Age, y	32.85±4.89	32.61±5.65	0.799
Body mass index, kg/m^2	22.03±3.89	21.92±2.53	0.876
Ethnicity			0.247
Chinese	133 (94.3)	32 (88.9)	
Non-Chinese	8 (5.7)	4 (11.1)	
Parity			0.796
Nulliparous	101 (71.6)	25 (69.4)	
Multiparous	40 (28.4)	11 (30.6)	
Mode of delivery			0.648
Normal vaginal delivery	91 (64.5)	24 (66.7)	
Vaginal enhanced delivery	24 (17.0)	4 (11.1)	
Fetal distress	7 (5.0)	1 (2.8)	
Lower segment Caesarean section	19 (13.5)	7 (19.4)	
Haemoglobinopathy			0.147
Thalassemia trait	22 (15.6)	6 (16.7)	
Other	8 (5.7)	6 (16.7)	
Blood transfusion prior to treatment	22 (15.6)	8 (22.2)	0.345
Blood loss, mL	550 (400-800)	400 (300-600)	<0.001
Baseline outcome			
Haemoglobin, g/dL	7.4 (7.05-7.8)	7.8 (7.15-7.9)	0.021
Ferritin, pmol/L (n=133 vs 17)	127 (81.5-209.5)	125 (82-203)	0.826
Multidimensional Fatigue Inventory			
Total score (n=131 vs 26)	54.02±14.23	55.85±15.84	0.82
Physical fatigue score (n=131 vs 26)	13.09±4.49	14.68±5.32	0.079
Week 2 outcome			
Haemoglobin, g/dL (n=125 vs 30)	10.55±0.9	10.15±1.05	0.035
Change in haemoglobin, g/dL (n=125 vs 30)	3.11±0.90	2.37±1.06	<0.001
Ferritin, pmol/L (n=124 vs 29)	599.5 (466.3-760.5)	109 (63.5-228)	<0.001
Multidimensional Fatigue Inventory			
Total score (n=112 vs 27)	49.22±14.23	50.37±13.8	0.706
Change in total score (n=106 vs 24)	-4.07±11.77	-3.54±13.49	0.192
Physical fatigue score (n=113 vs 26)	10.9±3.44	11.35±3.82	0.562
Change in physical fatigue score (n=106 vs 24)	-1.36±3.23	-1.08±3.39	0.71
Week 6 outcome			
Haemoglobin, g/dL (n=130 vs 35)	12.31±0.97	11.34±1.35	<0.001
Change in haemoglobin, g/dL (n=130 vs 35)	4.89±0.99	3.55±1.29	<0.001
Ferritin, pmol/L (n=129 vs 33)	189 (130-254)	100 (62-167.5)	<0.001
Multidimensional Fatigue Inventory			
Total score (n=108 vs 26)	46.17±14.06	48.61±10.4	0.467
Change in total score (n=102 vs 21)	-7.07±12.35	-7.24±15.83	0.957
Physical fatigue score (n=108 vs 26)	9.84±3.59	10.92±2.62	0.151
Change in physical fatigue score (n=102 vs 21)	-2.38±3.81	-2.29±4.43	0.918

* Data are expressed as mean ± standard deviation, No. (%) of patients, or median (interquartile range)

Only two (1.1%) patients reported mild adverse reactions (localised skin rash in one, palpitations and tachycardia in the other); both reactions resolved spontaneously.

Discussion

According to the Hong Kong Hospital Authority's annual report, the prevalence of primary postpartum haemorrhage (≥500 mL) reached a historic high of 14.7% in 2022[14]. Despite advances in prevention and treatment, the incidence of postpartum haemorrhage has significantly increased in recent decades[15]. This leads to higher rates of postpartum anaemia, which adversely affect women's physical and mental health-related quality of life[2].

Postpartum women treated with IV iron experience greater improvements in Hb levels than those treated with oral iron alone[1,5]. In our study, Hb concentrations at 6 weeks postpartum were approximately 1 g/dL higher in the IV iron group than in the oral iron group, consistent with findings from a meta-analysis[1]. Nonetheless, both IV and oral iron treatments produced comparable effects on maternal fatigue at 6 weeks postpartum, consistent with findings from a randomised controlled trial[16]. Fatigue may not be directly correlated with haemoglobin levels because multiple factors can influence maternal fatigue, including sleep deprivation from infant care, breastfeeding demands, hormonal changes, nutritional status, psychological stress, and postpartum depression. Additionally, mental fatigue and reduced motivation may contribute to the total MFI score.

First-line treatment with oral iron is often associated with gastrointestinal adverse effects, resulting in poor compliance. In contrast, IV iron enables rapid replenishment of iron stores and a faster rise in Hb levels while avoiding the gastrointestinal adverse effects linked to oral iron. Newer generations of IV iron preparations, such as iron isomaltoside (Monofer), are stable iron-carbohydrate complexes with a very low risk of severe allergic reactions. In our study, only two patients experienced mild adverse reactions, which resolved spontaneously; none developed severe adverse reactions or anaphylaxis. IV Monofer may therefore serve as an alternative to blood transfusion in haemodynamically stable patients with severe postpartum anaemia.

Although body weight is a key variable in the Ganzoni formula for calculating the optimal IV iron dosage[17], a Hong Kong study of IV iron therapy in gynaecological patients found no correlation between body weight and Hb increase[8]. Therefore, we adopted a dose-standardised protocol for IV iron administration, avoiding complex dose calculations and prolonged hospitalisation. This dose-standardised protocol effectively increased both Hb and ferritin levels in our patients, regardless of body weight or body mass index.

IV iron therapy can substantially reduce the need for blood transfusion by approximately 26%, thus lowering associated costs and risks[18]. It also requires less time and monitoring, and hospital stay, compared with blood transfusion. Unnecessary blood transfusion can be avoided and reserved for women who are haemodynamically unstable or have severe anaemic symptoms[19].

This study had several limitations. It was conducted at a single centre with a relatively small sample size, particularly in the oral iron group. Given its retrospective design, some data were missing due to incomplete documentation; thus, certain variables were reported using different denominators. The blood transfusion rate included both postnatal and antenatal patients, although the number of antenatal patients was small. Outcomes in the oral iron group may have been confounded by patients' adherence to treatment. Ferritin levels may also have been falsely elevated after delivery due to the inflammatory response associated with childbirth. Nevertheless, selection bias was minimal because treatment decisions and adverse event management followed a standardised protocol. Further large-scale, prospective, randomised controlled trials are warranted to validate the efficacy of IV iron therapy.

Conclusion

A single fixed dose of IV iron isomaltoside (Monofer) resulted in more rapid improvements in Hb levels and iron stores in women with severe postpartum anaemia, compared with oral iron, although MFI scores were similar between groups. IV iron is an effective alternative to blood transfusion for the management of severe postpartum anaemia.

Contributors

All authors designed the study, acquired the data, analysed the data, drafted the manuscript, and critically revised the manuscript for important intellectual content. All authors had full access to the data, contributed to the study, approved the final version for publication, and take responsibility for its accuracy and integrity.

Conflicts of interest

As an editor of the journal, WLL was not involved in the peer review process. Other authors have disclosed no conflicts of interest.

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Data availability

All data generated or analysed during the present study are available from the corresponding author on reasonable request.

Ethics approval

This study was approved by the Kowloon Central / Kowloon East Cluster Research Ethics Committee (reference: CIRB-2025-247-5). The patients were treated in accordance with the tenets of the Declaration of Helsinki. The requirement for patient consent was waived by the Committee due to the retrospective nature of the research.

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