Archives of Clinical Trials

Original Article

Safety and Efficacy of Feroxyl®, a Special Iron Bisglycinate Preparation in Improving Hemoglobin and Blood Biomarkers in Lebanese Patients with Iron Deficiency and Iron Deficiency Anemia: A Retrospective Chart Review

Patrick Choueiry[1], Pierre Haddad[2], Joe Baroudy[2], Rana Fassih[3], Salma Tradieh[3], Joseph Kareh[3], Wassim Jreij[3], Tanios Otayek[4], Imad Elias[4], Paul Makhlouf[4], Mariam Farhat[3], Jihad Ezzedine[3], Mohamad Hayek[5], Lina Jarrah[3], Rola Deeb[4] and Iman Akoush[4]

[1]MD, Medical Director Surveal Pharma, Lebanon
[2]MD, Family Doctor
[3]MD, Obstetrics and Gynecology
[4]MD, General Practitioner
[5]MD, General Surgeon

Correspondence
Patrick Choueiry
Medical Director, Surveal Pharma, Lebanon

- Received Date: 11 Mar 2025
- Accepted Date: 26 Mar 2025
- Publication Date: 28 Mar 2025

Abstract

Anemia is a widespread public health issue, with iron deficiency anemia (IDA) responsible for 50% of cases. This study evaluates the effectiveness of Feroxyl, a ferrous bisglycinate supplement enriched with vitamins, in improving hemoglobin and other blood biomarkers among a cohort of Lebanese patients with ID or IDA. A retrospective chart review of 593 patients showed significant improvements in hemoglobin (1.81 g/dL increase) and biomarkers like MCV, MCH, as well as ferritin after three months of supplementation. Vitamin D also significantly Increased. The supplement was well-tolerated, with mild side effects, making Feroxyl a promising treatment for IDA, particularly in low-resource settings.

Introduction

Anemia is a global public health problem affecting both developed and developing countries and is characterized by hemoglobin levels below 12.0 g/dL in women and 13.0 g/dL in men, and below 11.0 g/dL in pregnant women [1-3]. Iron deficiency from malnutrition is solely responsible for 50% of iron deficiency anemia (IDA) cases [4]. According to the World Health Organization (WHO), IDA affected around 25% of the global population (around 1.6. billion) [4]. IDA is most common in children and women; according to a 2015 report by the WHO, the prevalence of IDA was highest among preschoolers at 42.6%, followed by pregnant women at 38.2%, and non-pregnant women at 29.0% [5]. In the Eastern Mediterranean Region, most countries are not on track of meeting the sustainable development goals (SDGs) in achieving a 50% reduction in the prevalence of anemia, especially among women of reproductive age (WRA) [6]. In Lebanon for instance, anemia is found in 35.2% of pregnant women, 31.2% in WRA, and in 25% of children under 5 [6].

Iron is an essential element involved in a variety of critical functions, including oxygen transport, DNA synthesis, metabolic energy production, and cellular respiration [7]. Iron plays a vital role in the role of iron binding proteins, which deliver oxygen to various organs in mammals, and are crucial for the myelination of the spinal cord and the white matter of the central nervous system (CNS) [8]. Iron deficiency and IDA bear many adverse effects during pregnancy on women and neonates. Outcomes include low birth weight and premature labor; cognitive impairment and behavioral difficulties were also reported postpartum [9-12]. Diagnosis of IDA is mainly done through laboratory testing of serum ferritin levels.

Iron supplementation, be it oral, intravenous, or dialysate iron, is the mainstay management of IDA. Oral iron supplements, including ferrous (sulfate, fumarate, gluconate, glycine-sulfate) and ferric (protein-succinylate, mannitol-ovoalbumin, polymaltose complex) compounds are commonly used and are easily accessible, safe, and cost-effective, particularly in low-resource settings [13]. When oral supplementation falls short in cases where rapid replenishment is needed, ongoing blood loss, or inflammation, intravenous iron is

Citation: Choueiry P, Haddad P, Baroudy J, et al. Safety and Efficacy of Feroxyl®, a Special Iron Bisglycinate Preparation in Improving Hemoglobin and Blood Biomarkers in Lebanese Patients with Iron Deficiency and Iron Deficiency Anemia: A Retrospective Chart Review. Arch Clin Trials. 2025;5(1):04

usually administered [14-17]. Soluble ferric pyrophosphate is also administered through the dialysate solution in patients undergoing hemodialysis [13].

Feroxyl is a ferrous bisglycinate iron supplement used for iron deficiency anemia. This bisglycinate salt has been documented to be superior to other salts in terms of efficacy, bioavailability, and tolerability [18-20]. Feroxyl contains also 1,000 IU vitamin D, 400 µg of L-methylfolate, vitamin B12 and vitamin C. This paper aims to assess the impact or Feroxyl on hemoglobin and other relevant blood biomarkers in a cohort of anemic patients in Lebanon, a lower-middle income country.

Methodology

A retrospective chart review was conducted among Lebanese patients who have been prescribed Feroxyl (from Surveal Pharma Belgium) by their physicians between January 2023 and April 2024. Indications for oral iron prescription include iron deficiency with or without anemia, pregnancy supplementation, breast feeding supplementation, menorrhagia, menometrorrhagia, supplementation post myomectomy, and supplementation post hysterectomy. Sixteen physicians specializing in obstetrics, Gynecology, internal medicine, and General Practitioners were selected to recruit patients.

Patients were included if they were identified in the medical records as having iron deficiency anemia (hemoglobin below 11 g/dl) or iron deficiency without anemia (low ferritin, Hb > 11).

Data was retrospectively collected from medical records at baseline and 3 months after the initiation of oral supplementation. Data included sociodemographic characteristics (age, nationality, height, and weight), blood biomarkers (hemoglobin, MCV, MCH, MCHC, serum ferritin, and serum vitamin D). BMI was calculated for all participants. Additionally, patient reported adverse events whenever reported was documented and included metallic taste, nausea, vomiting, and diarrhea. KOBO Toolbox was used for data entry.

The study was an observational analysis of pre-existing medical records and did not involve direct contact with participants. In addition, each patient was assigned a unique, anonymized identification number for this study to ensure the confidentiality and privacy of the data collected.

Data analysis

The analysis was conducted using STATA 18. Descriptive statistics were initially conducted for sociodemographic and clinical characteristics in addition to blood biomarkers using the frequency and corresponding valid percentage. Paired sample t-test was conducted to reveal difference between blood biomarkers at baseline and last visit. Box plots were also created for each biomarker to better understand the distribution of the corresponding value. Linear regression model was generated for each biomarker adjusting for age and BMI. Statistical significance was assumed at p-value<0.05.

***Table 1**. Demographic and side effects profile of the sample*

Total sample=593	
Variable	
Age	35.04±12.94
Height	164.64±6.59
Weight	71.03±19.49
BMI	26.41±6.94
Side Effects	
Metalic taste	18(4.04%)
Constipation	45(10.09%)
Nausea	26(5.83%)
Vomiting	2(0.45%)

Results

Demographic characteristics

The sample studied included 593 participants, with a mean age of 35.04 years and an average BMI of 26.41. The side effects profile was as follows: 4% experienced a metallic taste, 10% experienced constipation, approximately 6% experienced nausea, and less than 1% experienced vomiting (Table1).

Blood samples characteristics

At the start of the study, 22% of the participants (n=129) had hemoglobin levels above 12g/dl. After 3 months of treatment, 61.55% (365) of the participants had hemoglobin levels above 12g/dl. Among the participants, 38.79% (n=230) experienced a change in hemoglobin levels of more than 2g/dl, and 29.01% (172) had a change between 1 and 2g/dl. The average change in hemoglobin levels was 1.81g/dl (1.28) for those with initial hemoglobin levels below 12g/dl, compared to 0.55g/dl (0.95) for those with hemoglobin levels above 12g/dl (p<0.001).

Table 2 presents significant changes in various blood parameters from baseline to three months (P<0.001). Hemoglobin levels increased from 11.27±5.87 to 12.52±2.16. Mean corpuscular volume (MCV) rose from 80.69±9.03 to 84.32±7.19, while mean corpuscular hemoglobin (MCH) improved from 29.23±4.47 to 30.87±4.09. Mean corpuscular hemoglobin concentration (MCHC) increased from 32.23±2.59 to 33.64±3.67. There was a significant rise in serum ferritin levels from 20.86±37.63 to 35.14±40.00. Additionally, serum vitamin D levels improved from 32.49±27.82 to 48.88±28.45.

The linear regression analysis shows that age has a significant positive association with changes in mean corpuscular hemoglobin (MCH, P=0.004) and serum vitamin D levels (P=0.03), while BMI has a significant negative association

***Table 2.** Comparison of the collected blood samples at baseline and 3 months*

Variable	Baseline	After 3 months	p-value
Hemoglobin (g/dl)	11.27±5.87	12.52±2.16	<0.001
MCV (fL)	80.69±9.03	84.32±7.19	<0.001
MCH (pg)	29.23±4.47	30.87±4.09	<0.001
MCHC (g/dl)	32.23±2.59	33.64±3.67	<0.001
Serum ferritin (ng/ml)	20.86±37.63	35.14±40.00	<0.001
Serum vitamin D (ng/ml)	32.49±27.82	48.88±28.45	<0.001

Table 2. *Linear regression of the difference in blood samples adjusting for age and BMI*

Variable	Hemoglobin	MCV	MCH	MCHC	Ferritin	Vitamin D
Age						
Coefficient	0.01	0.03	0.03	-0.01	0.07	0.24
95% CI	-0.03;0.05	-0.02;0.08	0.01;0.05	-0.05;0.03	-0.04;0.18	0.03;0.44
P-value	0.64	0.28	0.004	0.51	0.22	0.03
BMI						
Coefficient	-0.05	-0.04	-0.02	-0.08	-0.38	0.02
95% CI	-0.12;0.02	-0.12;0.05	-0.06;0.01	-0.15;-0.01	-0.59;-0.16	-0.68;0.72
P-value	0.19	0.42	0.21	0.03	0.001	0.96

with changes in mean corpuscular hemoglobin concentration (MCHC, P=0.03) and serum ferritin levels (P<0.001). Other blood parameters, such as hemoglobin, MCV, and the remaining variables, did not show significant associations with age or BMI.

Discussion

In this retrospective study, we aimed to investigate the effectiveness of the oral iron supplementation Feroxyl on a multi-center cohort of patients from a lower-middle income setting. Our findings indicate that 3 months after initiating Feroxyl therapy, there was a significant increase in hemoglobin and other blood parameters compared to the baseline laboratory tests.

Our study shows a significant increase of 1.25g/dl in hemoglobin levels on average despite a relatively high mean levels of hemoglobin at baseline (11.27g/dl). These results were reflected in other studies and across multiple age groups. In the study by Vir et al, 596 school and 437 non-school girls aged 10 to 19 years old, a 1.2g/dl increase in hemoglobin levels was documented [21]. In a randomized control trial conducted among workers aged 18 to 58 years, Mahanta et al showed an increase of 1.44g/dl in hemoglobin among the supervised group [22]. Both of these studies, similar to ours, were conducted in a lower-middle income country, India, which makes our results equally reliable.

The mean corpuscular volume (MCV) in our study increased on average by 3.6fL significantly. A study by Berber et al documented an MCV increase by almost 3fl in the Fe3+ group and around 10fL in the Fe2+ group [23]. Both studies showed a significant change in MCV, however our study had a larger sample size which could explain the differences observed in mean MCV levels. Overall, both studies showed similar results in blood parameters changes. The mean corpuscular hemoglobin concentration (MCHC) in our study increased by 1.41g/dl. This is comparable to the 1.7g/dl changes observed by Berber et al. Ferritin levels were also significantly increased in both studies. However, our cohort showed an increase of around 14ng/dl which is higher than that documented by Berber of 4ng/dl. This discrepancy can be explained by the fact that Berber used ferrous sulphate while Feroxyl contain ferrous bisglycinate. Studies have documented that ferrous bisglycinate displayed higher effectiveness and better absorption than the sulphate salt [24,25].

Feroxyl displayed a relatively safe adverse events profile. Ten percent of our cohort experienced constipation and 6% nausea. These results were comparable to a study Singh et al. showing that 7.8% and 8.9% of patients on ferrous bisglycinate experienced constipation and nausea, respectively [18]. These results were significantly lower than those caused by the sulphate salt, which shows a better gastrointestinal side effects profile for the bisglycinate salt [18].

It's important to note some limitations of our study. First, our cohort didn't assess how effective oral iron supplementation is for different conditions. Second, we didn't track the daily dose of Feroxyl or whether participants consistently took it. Third, not having a control group means we can't solely attribute any changes to the intervention without considering other factors. Fourth, relying on participants' self-reports could introduce bias in terms of adherence and dietary intake, affecting the outcomes. Also, the three-month study duration may not capture the long-term effects on hemoglobin levels. To address these limitations, future research should include a control group, track doses more thoroughly, and extend the follow-up period to evaluate long-term benefits.

Our retrospective chart review is based on real-world data, reflecting the variations in treatment outcomes, making our results reliable variations in a real-world setting, making our results reliable. The use of a multi-centered approach enhances the generalizability of our findings across different population subgroups within the lower-middle income setting. Furthermore, the significant improvements observed in hemoglobin, MCV, MCHC, and ferritin levels suggest that Feroxyl could be a viable option for managing iron deficiency anemia in similar settings.

The review found that Feroxyl was effective in improving the anemic condition of outpatients by significantly enhancing hemoglobin, ferritin and other blood parameters after a 3-month follow-up. These results highlight the potential of oral iron supplementation with Feroxyl as a practical intervention in areas with high prevalence of anemia or iron deficiency. The positive outcomes of this study could provide valuable insights for healthcare policies and guidelines aimed at tackling iron deficiency anemia in lower-middle-income countries.

References

1. Blanc M, Hureau JC. Catalogue critique des types de poissons du Muséum national d'Histoire naturelle (poissons à joues cuirassées). Publ Diverses Mus Natl Hist Nat. 1968;23:1-71.
2. Cappellini MD, Motta I. Anemia in clinical practice—definition and classification: does hemoglobin change with aging? Elsevier. 2015:261-269.
3. World Health Organization. Assessing the iron status of populations: including literature reviews. WHO. 2007.
4. World Health Organization. Worldwide prevalence of anaemia

1993-2005: WHO global database on anaemia. WHO. 2008.

5. World Health Organization. The global prevalence of anaemia in 2011. WHO. 2015.
6. Al-Jawaldeh A, Taktouk M, Doggui R, et al. Are countries of the Eastern Mediterranean Region on track towards meeting the World Health Assembly target for anemia? A review of evidence. Int J Environ Res Public Health. 2021;18(5):2449. doi:10.3390/ijerph18052449
7. Cappellini MD, Santini V, Braxs C, Shander A. Iron metabolism and iron deficiency anemia in women. Fertil Steril. 2022;118(4):607-614. doi:10.1016/j.fertnstert.2022.06.034
8. Soetan K, Olaiya C, Oyewole O. The importance of mineral elements for humans, domestic animals and plants: A review. Afr J Food Sci. 2010;4(5):200-222.
9. Kramer MS, Séguin L, Lydon J, Goulet L. Socioeconomic disparities in pregnancy outcome: why do the poor fare so poorly? Paediatr Perinat Epidemiol. 2000;14(3):194-210. doi:10.1046/j.1365-3016.2000.00273.x
10. Murray-Kolb LE. Iron and brain functions. Curr Opin Clin Nutr Metab Care. 2013;16(6):703-707. doi:10.1097/MCO.0b013e328365ae48
11. Milman N. Postpartum anemia II: prevention and treatment. Ann Hematol. 2012;91:143-154. doi:10.1007/s00277-011-1278-y
12. Beard J. Iron deficiency alters brain development and functioning. J Nutr. 2003;133(5 Suppl 1):1468S-1472S. doi:10.1093/jn/133.5.1468S
13. Muñoz M, Gómez-Ramírez S, Bhandari S. The safety of available treatment options for iron-deficiency anemia. Expert Opin Drug Saf. 2018;17(2):149-159. doi:10.1080/14740338.2018.1415328
14. Shepshelovich D, Rozen-Zvi B, Avni T, Gafter U, Gafter-Gvili A. Intravenous versus oral iron supplementation for the treatment of anemia in CKD: an updated systematic review and meta-analysis. Am J Kidney Dis. 2016;68(5):677-690. doi:10.1053/j.ajkd.2016.05.019
15. European Medicines Agency. New recommendations to manage risk of allergic reactions with intravenous iron-containing medicines. EMA. 2013.
16. Muñoz M, Breymann C, García-Erce JA, Gómez-Ramírez S, Comin J, Bisbe E. Efficacy and safety of intravenous iron therapy as an alternative/adjunct to allogeneic blood transfusion. Vox Sang. 2008;94(3):172-183. doi:10.1111/j.1423-0410.2007.01024.x
17. Auerbach M, Muñoz M. Intravenous iron for treating cancer-induced anemia: meeting an unmet need? Chin Clin Oncol. 2012;1(2):21-21. doi:10.3978/j.issn.2304-3865.2012.05.01
18. Singh S, Singh S, Lata S, Jain R, Bissa U, Ramanidevi T. Evaluation of efficacy and tolerability of ferrous bisglycinate tablets in comparison with ferrous sulphate tablets in patients with iron deficiency anemia. J Pharm Res. 2011;4:2836-2839.
19. Bovell-Benjamin AC, Viteri FE, Allen LH. Iron absorption from ferrous bisglycinate and ferric trisglycinate in whole maize is regulated by iron status. Am J Clin Nutr. 2000;71(6):1503-1509. doi:10.1093/ajcn/71.6.1503
20. Youssef AM, Shata AF, Kamal HM, El-Saied Y, Ali OF. A comparative study of efficacy, tolerability, and compliance of oral iron preparations for iron deficiency anemia in pregnant women. Am J Med Med Sci. 2014;4(6):244-249.
21. Vir SC, Singh N, Nigam AK, Jain R. Weekly iron and folic acid supplementation with counseling reduces anemia in adolescent girls: a large-scale effectiveness study in Uttar Pradesh, India. Food Nutr Bull. 2008;29(3):186-194.
22. Mahanta T, Trackroo A, Mahanta B. Effect of directly observed iron therapy (DOIT) in anaemia and productivity–A community-based intervention study in Dibrugarh, Assam. Indian J Appl Res. 2013;3(4):22-25.
23. Berber I, Diri H, Erkurt MA, Aydogdu I, Kaya E, Kuku I. Evaluation of ferric and ferrous iron therapies in women with iron deficiency anaemia. Adv Hematol. 2014;2014:297057.
24. Szarfarc SC, de Cassana LM, Fujimori E, Guerra-Shinohara EM, de Oliveira IM. Relative effectiveness of iron bis-glycinate chelate (Ferrochel) and ferrous sulfate in the control of iron deficiency in pregnant women. Arch Latinoam Nutr. 2001;51(1 Suppl 1):42-47.
25. Christensen JM, Ghannam M, Ayres JW. Effects of divalent amino acids on iron absorption. J Pharm Sci. 1984;73(9):1245-1248.