

EFFECTIVE CONTROL, TREATMENT AND PREVENTION OF ANEMIA IN HEART FAILURE AND DISEASES IN THE FERGANA VALLEY

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Abstract

This study examines anemia correction protocols in 284 cardiovascular patients across three clinical centers in the Fergana Valley during 2022-2024. Combined iron supplementation with erythropoiesis-stimulating agents demonstrated hemoglobin elevation from 98.4 g/L to 118.7 g/L over 16 weeks, alongside reduced hospitalization rates by 34% and improved functional capacity in NYHA class II-III patients with concurrent heart failure and iron deficiency anemia.

Keywords: anemia, heart failure, iron deficiency, cardiovascular diseases, erythropoiesis-stimulating agents, hemoglobin, ferritin, NYHA classification, Fergana Valley, cardiorenal syndrome, hospitalization, quality of life, ferrous sulfate, intravenous iron, treatment outcomes.

Introduction

Cardiovascular pathology remains the dominant cause of mortality in Uzbekistan's Fergana Valley, where demographic aging and metabolic comorbidities create particular challenges for clinical management. Anemia occurs in 37-48% of patients with chronic heart failure in this region, substantially worsening prognosis through reduced oxygen delivery, increased cardiac workload, and accelerated disease progression. The overlap between iron deficiency and inflammatory mechanisms in heart failure creates diagnostic complexity that regional healthcare systems struggle to address systematically. While international guidelines acknowledge anemia as a prognostic factor, practical implementation of correction strategies remains inconsistent across Central Asian clinical settings, where resource limitations and fragmented care pathways impede optimal outcomes.

Literature Review

Belenkov and Mareev's 2021 analysis of Russian heart failure registries documented anemia prevalence of 42% among hospitalized patients, with particularly severe outcomes in those presenting hemoglobin below 100 g/L. Fomin's Moscow cohort demonstrated that untreated anemia accelerates functional decline by 2.3-fold compared to adequately managed cases. Regional studies by Kamilova from Tashkent Medical Academy identified iron deficiency in 68% of Uzbek heart failure patients, considerably higher than European populations, potentially reflecting dietary patterns and chronic inflammatory states. Rakhmanov's work in Fergana documented that only 23% of anemic cardiac patients received targeted correction therapy, primarily due to diagnostic gaps rather than medication availability. These findings collectively establish that Central Asian cardiovascular populations face distinct anemia profiles requiring region-adapted management protocols beyond standard international recommendations.



Methodology

This prospective observational cohort study enrolled patients between January 2022 and March 2024 across three centers in Fergana, Margilan, and Kokand. The study population consisted of 284 adults aged 45-78 years with documented chronic heart failure (NYHA functional class II-III) and concurrent anemia defined as hemoglobin below 120 g/L for women and below 130 g/L for men. Inclusion criteria required stable heart failure medication regimens for at least eight weeks, left ventricular ejection fraction between 28% and 45%, and confirmed iron deficiency characterized by serum ferritin under 100 mcg/L or transferrin saturation below 20%. Patients were excluded if they demonstrated active bleeding, malignancy, severe renal impairment with creatinine clearance under 30 mL/min, recent blood transfusions within 90 days, or inflammatory conditions requiring immunosuppression. Participants received either oral ferrous sulfate 200 mg twice daily combined with ascorbic acid (n=156) or intravenous iron carboxymaltose 500-1000 mg depending on calculated deficit alongside subcutaneous erythropoietin-beta 50 IU/kg weekly for severe cases with hemoglobin below 90 g/L (n=128). Treatment allocation followed institutional protocols rather than randomization, reflecting real-world practice patterns. Primary endpoints measured hemoglobin concentration changes, serum ferritin levels, and transferrin saturation at baseline, 8 weeks, and 16 weeks. Secondary outcomes included six-minute walk distance, hospitalization frequency, NT-proBNP levels, and quality of life assessment using Minnesota Living with Heart Failure Questionnaire. Clinical evaluation occurred monthly with complete blood counts, iron panel assessments, and renal function monitoring. Adverse events were systematically recorded, particularly gastrointestinal intolerance with oral preparations and infusion reactions with parenteral iron. Statistical analysis employed paired t-tests for within-group comparisons and independent t-tests for between-group differences, with significance threshold set at $p < 0.05$. Multivariate regression adjusted for baseline ejection fraction, renal function, and diabetes status. The study protocol received approval from the Regional Medical Ethics Committee, and all participants provided written informed consent after thorough explanation of procedures and potential risks.

Results

Baseline characteristics showed mean age of 63.2 years with 58% male representation. Initial hemoglobin averaged 98.4 g/L in the oral supplementation group and 94.7 g/L in the combined intravenous plus erythropoietin group, reflecting more severe anemia in patients allocated to intensive therapy. Serum ferritin demonstrated profound depletion at 34.6 mcg/L and transferrin saturation measured just 14.3% across the cohort, confirming absolute iron deficiency as the predominant mechanism rather than anemia of chronic disease alone.

After 16 weeks, hemoglobin increased to 118.7 g/L in oral iron recipients and 126.3 g/L in the intravenous group, representing elevations of 20.3 g/L and 31.6 g/L respectively. The difference between treatment modalities reached statistical significance with $p = 0.003$, indicating superior efficacy of parenteral iron administration in this population. Ferritin rose to 112.4 mcg/L with oral therapy and 186.7 mcg/L with intravenous iron, while transferrin saturation improved to 22.8% and 28.4% respectively. These biochemical improvements translated to meaningful clinical changes, as 67% of patients in the intravenous group achieved target hemoglobin above 120 g/L compared to 43% receiving oral supplementation. Functional capacity measured by six-minute walk distance



improved from baseline 284 meters to 346 meters in oral iron patients and from 268 meters to 371 meters with combined parenteral therapy. This 103-meter improvement in the intensive treatment arm exceeded minimal clinically important difference thresholds and correlated with NYHA class improvement in 54% of these patients, compared to 31% improvement in the oral group. Hospitalization rates during the 16-week observation period reached 18% in oral iron recipients versus 11% in the intravenous cohort, representing a 34% relative risk reduction. NT-proBNP levels decreased by 28% from baseline in patients achieving hemoglobin above 115 g/L, suggesting reduced cardiac stress accompanying anemia correction. Adverse events occurred more frequently with oral supplementation, as 38% reported gastrointestinal symptoms including nausea, constipation, or epigastric discomfort, leading to treatment discontinuation in 12% of cases. Intravenous iron demonstrated better tolerance with only 7% experiencing mild infusion reactions, none requiring cessation. Three patients in the erythropoietin subgroup developed hypertension requiring medication adjustment, but no thromboembolic complications occurred during follow-up.

Discussion

The substantial hemoglobin improvements observed with both treatment modalities confirm that systematic anemia correction remains feasible within Fergana Valley's healthcare infrastructure, despite resource constraints compared to Western European centers. The superior outcomes achieved with intravenous iron and selective erythropoietin use align with findings from the FAIR-HF and CONFIRM-HF trials in European populations, yet our absolute hemoglobin changes exceeded those reported in these studies by approximately 8-12 g/L. This discrepancy likely reflects more severe baseline iron depletion in our cohort, where dietary iron intake remains inadequate and chronic inflammatory states from untreated infections contribute to functional deficiency. The 34% reduction in hospitalization rates carries substantial economic and quality-of-life implications for a region where hospital capacity remains strained and family caregiving burdens are significant. Previous Russian data suggested hospitalization reductions of 20-25% with anemia treatment, making our findings somewhat more optimistic than regional benchmarks. Whether this enhanced benefit stems from better treatment adherence, less comorbid complexity in our selected population, or genuinely superior protocol effectiveness requires validation through controlled trials rather than observational cohorts.

Functional capacity improvements exceeding 100 meters in six-minute walk distance represent clinically meaningful gains, as this magnitude correlates with reduced mortality risk in heart failure populations according to meta-analyses. The relationship between hemoglobin normalization and NT-proBNP reduction supports mechanistic theories that anemia correction decreases cardiac workload rather than merely improving exercise tolerance through peripheral oxygen delivery. However, our study design cannot definitively establish causality versus confounding from overall treatment optimization during the observation period. The high gastrointestinal intolerance with oral iron supplementation, affecting 38% of patients, substantially exceeds rates reported in younger populations without heart failure, likely reflecting delayed gastric emptying, polypharmacy interactions, and baseline dyspepsia common in this demographic. These findings argue for preferential use of intravenous preparations in Central Asian heart failure populations where treatment adherence already poses challenges due to complex medication regimens and limited



patient education infrastructure. Limitations include the non-randomized treatment allocation, which introduces selection bias despite our statistical adjustments. The relatively short 16-week follow-up prevents assessment of long-term sustainability and safety, particularly regarding iron overload risks with repeated parenteral dosing. Absence of bone marrow examination means we cannot definitively exclude other anemia etiologies, though the robust response to iron supplementation argues against significant contributions from alternative mechanisms in most cases.

Structured anemia management protocols incorporating intravenous iron therapy demonstrate substantial clinical benefits in Fergana Valley heart failure populations, with hemoglobin improvements translating to enhanced functional capacity and reduced hospitalization burden. Regional implementation requires systematic screening, preferential parenteral iron use, and integration with existing heart failure care pathways to maximize population-level impact within Central Asian healthcare systems.

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