OPEN ACCESS Freely available online

Journal of Hematology & Thromboembolic Diseases

Short Communication

Advances in Iron-Restricted Erythropoiesis and Its Implications for Iron Therapy

Forster Sarah*

Department of Hematology, Mulungushi University, Kabwe, Zambia

DESCRIPTION

Recent insights into the connection between erythropoietin, iron, and erythropoiesis in individuals with blood loss anemia, whether or not they undergo recombinant human erythropoietin therapy, carry significant implications for patient care. In instances of substantial blood loss, or when erythropoietin therapy is employed, or both, there is observable evidence of iron-restricted erythropoiesis, even in the presence of stored iron and oral iron supplementation [1]. Renal dialysis patients receiving erythropoietin therapy and intravenous iron treatment exhibit hematologic responses, with serum ferritin levels reaching upto 400 μg/L. This underscores the inadequacy of traditional biochemical markers for assessing storage iron in anemic patients with chronic diseases. Modern measurements utilizing automated counters to evaluate reticulocyte indices have the potential to detect erythropoiesis restricted by iron.

While assays for serum erythropoietin and the transferrin receptor prove valuable in clinical research, their roles in routine clinical practice remain undefined. The emergence of safer intravenous iron preparations enables controlled studies to assess their efficacy in patient's and various clinical scenarios have functioned as "natural experiments," advancing our comprehension of the interplay among erythropoietin, iron, and the erythropoietic response to anemia in humans. Approximately two decades ago, Finch provided a comprehensive overview, primarily drawing insights from studies involving healthy individuals, those with hereditary hemolytic anemias, and patients with hemochromatosis. Under conditions of basal erythropoiesis in normal subjects, plasma iron turnover, indicative of marrow erythropoietic response, remains relatively unaffected, irrespective of transferrin saturation levels [2]. Conversely, individuals with congenital hemolytic anemia, experiencing chronically elevated erythropoiesis, exhibit a response influenced and constrained by serum iron levels and transferrin saturation. Hemochromatosis patients, subjected to serial phlebotomies, mount significant erythropoietic responses attributed to sustained high serum iron and transferrin saturation levels.

Autologous phlebotomy-induced blood loss anemia

Patients undergoing autologous blood phlebotomy may donate approximately 10.5 mL/kg (450 ± 45 mL) blood as frequently as twice a week until 72 hours before surgery, with routine donations occurring once a week. Oral iron supplements are typically prescribed. This iatrogenic blood loss prompts an increase in endogenous erythropoietin levels, significantly elevated over basal levels but within the normal range (4-26 μm/mL). The resulting erythropoietic response is modest, with estimated red blood cell volume expansion surpassing basal rates, highlighting the efficacy of this blood conservation practice. More aggressive phlebotomy, up to 2 units weekly, elicits a more substantial endogenous erythropoietin response [3]. The relationship between change in hemoglobin levels and erythropoietin response aligns with predictions from phlebotomy experiments in normal subjects.

Erythropoiesis facilitated by erythropoietin therapy

Clinical trials demonstrate a dose-response relationship between erythropoietin and red blood cell expansion. Even "very low" dose erythropoietin therapy in autologous blood donors results in clinically significant erythropoiesis. The response varies widely but is not influenced by patient gender or age suggesting other factors like chronic disease or iron-restricted erythropoiesis contributes to this variability. Studies in patients with anemia of chronic disease further underscore the comparable erythropoietic responses between endogenous erythropoietin-mediated erythropoiesis and erythropoietin therapy.

Iron-restricted erythropoiesis and iron therapy

The response of erythropoiesis to aggressive autologous phlebotomy, driven by endogenous erythropoietin, exhibits a threefold increase. Intriguingly, basal iron stores do not correlate with this level of erythropoiesis, suggesting that storage iron sufficiently maintains serum iron and transferrin saturation for erythron requirements [4]. Oral iron supplementation demonstrates limited efficacy, while intravenous iron proves ineffective under these conditions. Even in patients with

Correspondence to: Forster Sarah, Department of Hematology, Mulungushi University, Kabwe, Zambia, E-mail: forsarah@ster.com

Received: 01-Nov-2023, Manuscript No. JHTD-23-28427; **Editor assigned:** 03-Nov-2023, Pre QC No. JHTD-23-28427 (PQ); **Reviewed:** 17-Nov-2023, QC No. JHTD-23-28427; **Revised:** 24-Nov-2023, Manuscript No. JHTD-23-28427 (R); **Published:** 01-Dec-2023, DOI: 10.35248/2329-8790.23.11.574.

Citation: Sarah F (2023) Advances in Iron-Restricted Erythropoiesis and Its Implications for Iron Therapy. J Hematol Thrombo Dis.11:574.

measurable storage iron during erythropoietin therapy, iron-restricted erythropoiesis becomes apparent, with a substantial increase in gastrointestinal iron absorption counteracted by a decrease of up to 50% in serum ferritin and transferrin saturation levels. Hematological changes, such as a fourfold surge in erythropoietic activity, declining reticulocyte counts, and the appearance of hypochromic red cells, underscore the impact of erythropoietin therapy. The study of hemochromatosis patients reinforces the notion of iron-restricted erythropoiesis in erythropoietin-treated individuals.

Factors influencing erythropoietic response

Basal red cell precursor mass acts as a constraining factor with half-maximal hemoglobin synthesis achievable with as few as 50 molecules of erythropoietin per target cell. The biological response is maximized at lower erythropoietin concentrations than needed to saturate all erythropoietin-binding sites. Optimal reticulocyte responses occur with a single erythropoietin dose of 1800 U/kg in healthy subjects, and multiple-dose regimens prove more effective in mobilizing storage iron than single-dose regimens. A 72-hour interval between erythropoietin administrations surpasses a 24-hour interval. Erythropoietin therapy triggers the gradual expansion of erythroblast mass, meeting acute and chronic demands for erythropoiesis [5].

Blood loss and iron therapy

In patients with blood loss anemia, iron-restricted erythropoiesis is clinically significant, irrespective of measurable storage iron. While oral iron suffices for endogenous erythropoietin-mediated red blood cell expansion, it may not prevent iron-restricted erythropoiesis during erythropoietin therapy. Intravenous iron enables a fivefold erythropoietic response to significant blood loss anemia in healthy individuals. However, challenges arise in achieving higher hemoglobin production rates unless red marrow expands into the yellow marrow space. Intravenous iron therapy in patients not undergoing erythropoietin therapy may result in iron sequestration in the reticuloendothelial system, limiting its availability for erythropoiesis

Anemia of chronic renal failure or chronic disease

Erythropoietin therapy's success in addressing anemia related to chronic renal failure provides insights into erythropoietin, iron metabolism, and erythropoiesis. Anemic dialysis patients may exhibit hyporesponsiveness to oral iron therapy due to factors like aluminum toxicity and iron deficiency [6]. Intravenous iron administration becomes a standard approach in these patients, with significant reductions in erythropoietin dosage. The efficacy of intravenous iron in patients with chronic disease underscores the complexity of iron-restricted erythropoiesis, requiring specialized treatment approaches [7,8]. These insights into iron-restricted erythropoiesis and its interplay with erythropoietin therapy pave the way for refined treatment strategies and further investigations to optimize patient outcomes.

CONCLUSION

Advancements in laboratory techniques for assessing iron-restricted erythropoiesis, coupled with clinical trials involving blood phlebotomy and erythropoietin therapy, have enhanced our comprehension of the intricate relationship among erythropoietin, iron, and erythropoiesis. Newly automated counters measuring hematologic indices and reticulocyte parameters exhibit promise in evaluating iron-restricted erythropoiesis, yet further investigations are imperative to ascertain their precise roles in conjunction with iron and erythropoietin therapy. While erythropoietin and transferrin receptor assays prove valuable in clinical research, their applications in routine clinical practice lack well-defined parameters.

REFRENCES

1. Crosby WH. The metabolism of hemoglobin and bile pigment in hemolytic disease. Am J Med. 1955;18(1):112-122.
2. Goodnough LT, Mercuriali F, Kasper SM, Buzello W. Compensatory eythropoiesis during routine autologous blood donation. Transfusion. 1998;38(6):613-615.
3. Goodnough LT, Price TH, Parvin CA, Friedman KD, Vogler WR, Khan N, et al. Erythropoietin response to anaemia is not altered by surgery or recombinant human erythropoietin therapy. Br J Haematol. 1994;87(4):695-699.
4. Price TH, Goodnough LT, Vogler WR, Sacher RA, Hellman RM, Johnston MF, et al. The effect of recombinant human erythropoietin on the efficacy of autologous blood donation in patients with low hematocrits: A multicenter, randomized, double-blind, controlled trial. Transfusion. 1996;36(1):29-36.
5. Goodnough LT, Marcus RE. The erythropoietic response to erythropoietin in patients with rheumatoid arthritis. J Lab Clin Med. 1997;130(4):381-386.
6. Schreiber S, Howaldt S, Schnoor M, Nikolaus S, Bauditz J, Gasché C, et al. Recombinant erythropoietin for the treatment of anemia in inflammatory bowel disease. N Engl J Med. 1996;334(10):619-624.
7. Biesma DH, Kraaijenhagen RJ, Poortman J, Marx JJ, van De Wiel A. The effect of oral iron supplementation on erythropoiesis in autologous blood donors. Transfusion. 1992;32(2):162-165.
8. Biesma DH, Wiel AV, Beguin Y, Kraaijenhagen RJ, Marx JJ. Erythropoietic activity and iron metabolism in autologous blood donors during recombinant human erythropoietin therapy. Eur J Clin Invest. 1994;24(6):426-432.