Iron Replacement Therapy and Anemia Associated With Chronic Infectious Diseases in Sub-Saharan Africa

To the Editor—We read with interest the article by Minchella and colleagues, who prospectively studied anemia (baseline prevalence, 67%) in patients with tuberculosis in The Gambia [1]. Although the most common etiology was immune-mediated anemia of chronic disease (ACD), iron deficiency anemia (IDA) and combined anemia (ACD + IDA) were also frequently observed. Whereas ACD typically resolved with successful tuberculosis treatment alone, IDA and ACD + IDA did not. At baseline, patients had high serum levels of hepcidin, the master regulator of iron homeostasis. Such high levels are predictive of nonresponsiveness to oral iron replacement therapy [2] due to its combined effects of inhibiting duodenal iron absorption and causing iron sequestration. However, since levels reduced to near normal after 2 months of tuberculosis treatment, the authors suggested that iron-based interventions for anemia might be effective from this time-point.

The data presented by Minchella and colleagues may be informative with regard to the management of anemia associated with other chronic infectious diseases in sub-Saharan Africa, including human immunodeficiency virus (HIV). We recently reported on the prevalence of anemia among HIV-infected patients (n = 814) in South Africa and on the recovery of hemoglobin levels during antiretroviral therapy (ART) [3]. During the first year of ART, the overall prevalence of anemia decreased from 71% to 27% and the prevalence of moderate/severe anemia decreased from 43% to 8%. Thus, although ART was associated with substantial recovery of hemoglobin levels, anemia persisted in an important subset of patients. In multivariable analysis, the factor most strongly associated with persistent anemia was persistence of erythrocyte microcytosis (mean corpuscular volume <80 fl) during ART.

ART is accompanied by rapid and profound reductions in systemic immune activation as plasma HIV load is suppressed and opportunistic infections resolve. Thus, in light of the data presented by Minchella and colleagues, we suspect that the hemoglobin recovery observed in our cohort was likely to be largely attributable to resolution of immune-mediated ACD and that the persistence of anemia in a subset of patients was due to IDA or ACD + IDA.
Iron replacement therapy is simple, inexpensive, widely available, and effective for IDA outside the context of inflammatory conditions such as chronic infection. However, it is thought that iron therapy could also potentially worsen clinical outcomes by functioning as a readily available essential nutrient for invading microbial pathogens and through immune impairment [4]. Indeed, the growth of a large number of infectious pathogens is stimulated by iron excess [5]. For example, risk of tuberculosis disease as well as subsequent tuberculosis treatment outcomes are directly related to iron status [6]. Thus, iron replacement therapy should only be used with appropriate understanding of the potential risks and benefits.

Although HIV-related anemia is common, it is associated with considerable morbidity and is an important predictor of mortality risk, there are no normative management guidelines for resource-limited settings. In those with severe anemia, a blood transfusion may be required, although some evidence suggests that transfusions may be associated with increased HIV disease progression and mortality [7]. Iron supplementation improved anemia and immunity in HIV-infected children in Malawi, but was also associated with an increased risk of malaria [8]. Although similar randomized studies among HIV-infected adults in sub-Saharan Africa are lacking, a small study in Kenya found no adverse effect of iron supplementation on plasma HIV RNA load [9]. However, in West Africa, elevated iron status among HIV-infected adults independently predicted mortality during long-term follow-up [10].

While ART is the key therapeutic intervention for HIV-related anemia, descriptive studies similar to that conducted by Minchella and colleagues are needed to carefully define the relative contributions of ACD and IDA among HIV-infected patients in sub-Saharan Africa and at what stage patients receiving ART have sufficient suppression of inflammation as to become responsive to iron supplementation.

**Notes**

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**Andrew D. Kerkhoff1,2,3 and Stephen D. Lawn4,5**

1George Washington University School of Medicine and Health Sciences, District of Columbia; 2Department of Global Health, Academic Medical Center, Amsterdam Institute for Global Health and Development, University of Amsterdam, The Netherlands; 3Desmond Tutu HIV Centre, Institute of Infectious Disease and Molecular Medicine, Faculty of Health Sciences, University of Cape Town, South Africa; and 4Department of Clinical Research, Faculty of Infectious and Tropical Diseases, London School of Hygiene and Tropical Medicine, United Kingdom

**References**


Correspondence: Andrew D. Kerkhoff, MSc, 2300 I St NW, Washington, D.C. 20037 (andrewkerkhoff@gmail.com). Clinical Infectious Diseases® 2015;60(9):1438–9 © The Author 2015. Published by Oxford University Press on behalf of the Infectious Diseases Society of America. All rights reserved. For Permissions, please e-mail: journals.permissions@oup.com. DOI: 10.1093/cid/civ063