Killing two birds with one stone: The potential of iron supplementation in Chinese HFrEF patients

Chia Siang Kow[a,*], Dinesh Sangarran Ramachandram[b], Syed Shahzad Hasan[c,d]

[a]School of Pharmacy, International Medical University, Kuala Lumpur, Malaysia; [b]School of Pharmacy, Monash University Malaysia, Bandar Sunway, Selangor, Malaysia; [c]School of Applied Sciences, University of Huddersfield, Huddersfield, United Kingdom; [d]School of Biomedical Sciences & Pharmacy, University of Newcastle, Callaghan, NSW, Australia

DEAR EDITOR,

We read with interest the study by Sung et al,[1] which aimed to assess the prevalence and significance of iron deficiency (ID) in Taiwanese patients with heart failure and reduced ejection fraction (HFrEF). Among the 3612 included HFrEF patients, 43.6% were found to have ID, irrespective of their anemia status. In fact, we believe that ID might be even more prevalent in this cohort of HFrEF patients than reported in the study. This assumption is based on previous research demonstrating that ferritin levels might not always accurately indicate low iron stores in this population. For instance, in a 2006 series of 37 patients with advanced HF and anemia, most of them (73%) showed no stainable bone marrow iron (indicating ID), despite only two of the iron-deficient patients having reduced serum ferritin levels.[2]

While the findings underscore the critical importance of carefully monitoring iron status in HFrEF patients, it is noteworthy that only 18.4% of the HFrEF patients in this study underwent complete ID assessment at baseline. However, we are encouraged by the observation that the rate of iron profile testing was significantly higher among patients using renin-angiotensin system (RAS) inhibitors. Specifically, angiotensin-converting enzyme (ACE) inhibitors, known for their beneficial effects on patient survival in heart failure, have been associated with incidence of anemia. In the landmark enalapril trial (Studies of Left Ventricular Dysfunction [SOLVD] study[3]) which involved patients with left ventricular dysfunction randomly assigned to either enalapril or placebo, it was reported that at 1 year after randomization, the rate of new anemia was significantly higher in the enalapril group (11.3% vs 7.9% with placebo). The effect of ACE inhibitors on hematocrit may be mediated by N-Acetyl-Seryl-Aspartyl-Proline (Ac-SDKP) (goralatide), a tetrapeptide that inhibits erythropoiesis. As Ac-SDKP is metabolized by ACE, its accumulation in the presence of an ACE inhibitor may inhibit erythropoiesis and contribute to the observed anemia.

Undoubtedly, HFrEF patients with ID should receive iron supplementation, as numerous trials[4] have demonstrated its beneficial effects in such cases. Nonetheless, it may be prudent to further explore the possibility of routine iron supplementation in all Chinese HFrEF patients who are receiving ACE inhibitors (not all patients may have access to sacubitril/valsartan due to cost considerations). Interestingly, dry cough has been reported in a significant proportion of patients treated with ACE inhibitors, and observations indicate that Chinese patients may experience a higher incidence of cough compared with other racial groups. Notably, iron supplementation has been shown to mitigate the ACE inhibitors-induced cough, as reported in a randomized trial.[5]

The significant prevalence of ID among HFrEF patients emphasizes the need for routine monitoring and timely intervention. Considering the potential impact of ACE inhibitors on hematocrit and the observed association with anemia, exploring routine iron supplementation for all Chinese HFrEF patients receiving ACE inhibitors may offer a dual benefit, not only addressing ID but potentially mitigating ACE inhibitor-induced cough. Further investigations and clinical trials in this area hold promise for optimizing therapeutic strategies and ultimately improving the quality of life for Chinese HFrEF patients.

REFERENCES

1. Sung HP, Hsu CY, Lee YH, Lin PL, Liao CT, Chung FP, et al. Iron deficiency in Taiwanese patients with heart failure and reduced ejection fraction*J Chin Med Assoc* 2023;86:725–31.
2. Nanas JN, Matsouka C, Karageorgopoulos D, Leonti A, Tsolakis E, Drakos SG, et al. Etiology of anemia in patients with advanced heart failure*J Am Coll Cardiol* 2006;48:2485–9.
3. Ishani A, Weinhandl E, Zhao Z, Gilbertson DT, Collins AJ, Yusuf S, et al. Angiotensin-converting enzyme inhibitor as a risk factor for the development of anemia, and the impact of incident anemia on mortality in patients with left ventricular dysfunction*J Am Coll Cardiol* 2005;45:391–9.
4. Song Z, Tang M, Tang G, Fu G, Ou D, Yao F, et al. Oral iron supplementation in patients with heart failure: a systematic review and meta-analysis*ESC Heart Fail* 2022;9:2779–86.
5. Lee SC, Park SW, Kim DK, Lee SH, Hong KP. Iron supplementation inhibits cough associated with ACE inhibitors*Hypertension* 2001;38:166–70.

*Address correspondence. Dr Chia Siang Kow, School of Pharmacy, International Medical University, 126, Jalan Jalil Perkasa, Bukit Jalil, Kuala Lumpur, Malaysia. E-mail address: chiasiang_93@hotmail.com (C.S. Kow).

Conflicts of interest: The authors declare that they have no conflicts of interest related to the subject matter or materials discussed in this article.

Journal of Chinese Medical Association. (2023) 86: 945.

Received August 01, 2023; accepted August 2, 2023.

doi: 10.1097/JCMA.0000000000000984