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LETTER TO THE EDITOR

Letter

Response to Does pumping iron bring gains? A review of the role of intravenous iron in perioperative blood management

I read the review article by Robinson et al.,¹ *Does pumping iron bring gains? A review of the role of intravenous iron in perioperative blood management,* with interest. The review provided an appealing summary of the role of intravenous iron in perioperative blood management. However, there were some important omissions.

The review stated, "Currently, there is a paucity in robust evidence supporting this practice." Since the review was performed in 2021, this statement is dated. This year alone, several articles supporting evidence for using parenteral iron to treat preoperative anaemia have been published. For example, a large risk-adjusted, propensity-matched retrospective cohort analysis over 20 years (2003–2023) by Choi et al.² showed that preoperative intravenous iron was associated with lower 30-day postoperative mortality and morbidity, higher 30-day postoperative haemoglobin, and a reduced incidence of red blood cell transfusions.

Robinson et al.¹ correctly highlighted the vital shortcomings of the Richards et al.³ PREVENTT study; however, these must be considered before discarding the role of intravenous iron in all patients with preoperative iron deficiency anaemia. Notwithstanding the limitations, the findings of Choi et al.² provide promising evidence to consider intravenous iron as a favourable alternative to red blood cell transfusion in iron-deficient anaemic patients in the perioperative setting.

Moreover, Robinson et al.¹ stated that only two intravenous iron formulations are available in South Africa: iron sucrose (Venofer®) and iron dextran (CosmoFer®). This is not accurate. Ferric derisomaltose (Monofer®, Acino Pharma) and ferric carboxymaltose (Ferinject®, Aspen), both suited to total dose infusions, are freely available in the South African private sector. Iron sucrose is also available from two other suppliers: Actor Pharma (Rautevene®) and Innovata Pharmaceuticals (Innofer®).

Readers should note the availability of ferric derisomaltose and ferric carboxymaltose in South Africa, as these iron preparations are both effective and safe in patients with iron deficiency anaemia.^{4,5} While cost may be a concern, the role of intravenous iron therapy in perioperative patient blood management may

be particularly relevant in low- to middle-income countries, where the prevalence of iron deficiency anaemia is high, and blood shortages are common.⁶⁻⁸ Screening for iron deficiency before major surgery, especially in high-risk groups, should be the standard of care, and treatment with parenteral iron should start timeously.^{2,9}

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References

- Robinson GRN, Breedt A, Oghenetega CON, Chetty S. Does pumping iron bring gains? A review of the role of intravenous iron in perioperative blood management. South Afr J Anaesth Analg. 2024;30(1):25-31. https://doi. org/10.36303/SAJAA.3013.
- Choi UE, Nicholson RC, Thomas AJ, et al. A propensity-matched cohort study of intravenous iron versus red cell transfusions for preoperative iron-deficiency anemia. Anesth Analg. 2024;139(5):969-77. https://doi.org/10.1213/ ANE.0000000000000974.
- Richards T, Baikady RR, Clevenger B, et al. Preoperative intravenous iron to treat anaemia before major abdominal surgery (PREVENTT): a randomised, doubleblind, controlled trial. Lancet. 2020;396(10259):1353-61. https://doi.org/10.1016/ S0140-6736(20)31539-7.
- Kalra PA, Bhandari S. Efficacy and safety of iron isomaltoside (Monofer) in the management of patients with iron deficiency anemia. Int J Nephrol Renovasc Dis. 2016;9:53-64. https://doi.org/10.2147/JJNRD.S89704.
- Naqash A, Ara R, Bader GN. Effectiveness and safety of ferric carboxymaltose compared to iron sucrose in women with iron deficiency anemia: phase IV clinical trials. BMC Womens Health. 2018;18(6):1-10. https://doi.org/10.1186/ s12905-017-0506-8.
- Raykar NP, Makin J, Khajanchi M, et al. Assessing the global burden of hemorrhage: the global blood supply, deficits, and potential solutions. SAGE Open Med. 2021;9:20503121211054995. https://doi. org/10.1177/20503121211054995.
- Martin M. Experts suggest innovations to address global blood crisis: short-term strategies could improve care for people in world's 'blood deserts' [Internet]. Harvard Medical School; 2024. Available from: https://hms.harvard.edu/news/ experts-suggest-innovations-address-global-blood-crisis. Accessed 4 November 2024.
- Dorsamy V, Bagwandeen C, Moodley J. The prevalence, risk factors and outcomes of anaemia in South African pregnant women: a systematic review and meta-analysis. Syst Rev. 2022;11(16). https://doi.org/10.1186/ s13643-022-01884-w.
- Iolascon A, Andolfo I, Russo R, et al. Recommendations for diagnosis, treatment, and prevention of iron deficiency and iron deficiency anemia. Hemasphere. 2024;8(7):e108. https://doi.org/10.1002/hem3.108.

Response

Dear Prof. Spijkerman,

We appreciate the opportunity to respond to the letter regarding our article, *Does pumping iron bring gains? A review of the role of intravenous iron in perioperative blood management* (Southern African Journal of Anaesthesia and Analgesia, 2024). We sincerely thank the author for their interest and insightful comments.

Perioperative blood management focuses on improving patient outcomes while saving healthcare resources and reducing costs. Intravenous iron therapy (IVIT) has been popularised to improve perioperative patient blood management. Our review article intended to highlight the evidence at the time, investigating the role of IVIT in the perioperative period.

The study by Choi et al.,² published in 2023, raises uncertainty about the role of IVIT, as the findings contrast with the conclusions of the prospective multicentre PREVENTT trial.¹ While Choi et al.'s² findings of the reduction in perioperative morbidity and mortality and the lower risk of postoperative transfusion are encouraging, we believe this reinforces our review's statement that there is still a need for a large-scale prospective randomised controlled trials on the subject.

Despite the Choi et al.² study including data collected over 20 years, it must be noted that this retrospective study did not include many important factors in its analysis. These include the timing of therapy before surgery, transfusion triggers and targets, the formulations of IVIT used, and the cumulative dose of intravenous iron used in each patient. Consequently, the correct IVIT regimen used to attain the results cannot be inferred from their study.

Further, the retrospective cohort by Choi et al.² compared the preoperative treatment of iron deficiency anaemia with intravenous iron versus blood transfusion. In contrast to other studies investigating the role of preoperative IVIT, their study focused on iron deficiency anaemia. While preoperative anaemia is associated with increased mortality, current evidence also suggests that liberal blood transfusion is not superior to restrictive blood transfusion and has been associated with increased mortality.²⁻⁷ There is no argument that preoperative iron deficiency anaemia should not be treated or that it should rather be treated with blood transfusion. The approximate reduction in mortality by 40% found by Choi et al.² highlights the deleterious effects of blood transfusion and the safety of IVIT.

In consideration, we stand by our statement that there is currently insufficient evidence to support preoperative intravenous iron in patients with anaemia.⁸ This is supported by the findings of several meta-analyses published since our review. ⁹⁻¹²

Regarding the description of available IVIT formulations in South Africa, it must be noted that the author of this letter is correct. Many other formulations of intravenous iron are available in the private healthcare sector. The two mentioned in our review (Venofer® and Cosmofer®) are the available formulations in the

state healthcare sector, which should have been clarified in the review.

Regards,

Dr. GRN Robinson, on behalf of all co-authors

References

- Richards T, Baikady RR, Clevenger B, et al. Preoperative intravenous iron to treat anaemia before major abdominal surgery (PREVENTT): a randomised, doubleblind, controlled trial. Lancet. 2020;396(10259):1353-61. https://doi.org/10.1016/ S0140-6736(20)31539-7.
- Choi UE, Nicholson RC, Thomas AJ, et al. A propensity-matched cohort study of intravenous iron versus red cell transfusions for preoperative iron-deficiency anemia. Anesth Analg. 2024;139(5):969-77. https://doi.org/10.1213/ ANE.0000000000006974.
- Rao SV, Jollis JG, Harrington RA, et al. Relationship of blood transfusion and clinical outcomes in patients with acute coronary syndromes. JAMA. 2004;292(13):1555-62. https://doi.org/10.1001/jama.292.13.1555.
- Cooper HA, Rao SV, Greenberg MD, et al. Conservative versus liberal red cell transfusion in acute myocardial infarction (the CRIT Randomized Pilot Study). Am J Cardiol. 2011;108(8):1108-11. https://doi.org/10.1016/j. amjcard.2011.06.014.
- Chatterjee S, Wetterslev J, Sharma A, Lichstein E, Mukherjee D. Association of blood transfusion with increased mortality in myocardial infarction: a meta-analysis and diversity-adjusted study sequential analysis. JAMA Intern Med. 2013;173(2):132-9. https://doi.org/10.1001/2013.jamainternmed.1001.
- Nixon CP, Sweeney JD. Severe iron deficiency anemia: red blood cell transfusion or intravenous iron? Transfusion. 2018;58(8):1824-6. https://doi.org/10.1111/ trf 14819
- Odutayo A, Desborough MJR, Trivella M, et al. Restrictive versus liberal blood transfusion for gastrointestinal bleeding: a systematic review and meta-analysis of randomised controlled trials. Lancet Gastroenterol Hepatol. 2017;2(5):354-60. https://doi.org/10.1016/S2468-1253(17)30054-7.
- Robinson GRN, Breedt A, Oghenetega CON, Chetty S. Does pumping iron bring gains? A review of the role of intravenous iron in perioperative blood management. South Afr J Anaesth Analg. 2024;30(1):25-31. https://doi. org/10.36303/SAJAA.3013.
- Sinclair RCF, Bowman MJA, Moppett IK, Gillies MA. Perioperative intravenous iron to treat patients with fractured hip surgery: a systematic review and meta-analysis. Health Sci Rep. 2022;5(3):e633. https://doi.org/10.1002/hsr2.633.
- Low WX, Friend H, Dulleston J, et al. Outcomes of perioperative intravenous iron infusion in femoral fracture surgery: a systematic review and meta-analysis of randomised controlled trials. Surgeon. 2024;22(5):e171-80. https://doi. org/10.1016/j.surge.2024.07.005.
- Meyer J, Cirocchi R, Di Saverio S, et al. Pre-operative iron increases haemoglobin concentration before abdominal surgery: a systematic review and meta-analysis of randomized controlled trials. Sci Rep. 2022;12(2158). https://doi.org/10.1038/ s41598-022-05283-y.
- Liu H-M, Tang X-S, Yu H, Yu H. The efficacy of intravenous iron for treatment of anemia before cardiac surgery: an updated systematic review and meta-analysis with trial sequential analysis. J Cardiothorac Surg. 2023;18(16). https:// doi.org/10.1186/s13019-023-02119-2.Nixon CP, Sweeney JD. Severe iron deficiency anemia: red blood cell transfusion or intravenous iron? Transfusion. 2018;58(8):1824-6. https://doi.org/10.1111/trf.14819.
- Odutayo A, Desborough MJR, Trivella M, et al. Restrictive versus liberal blood transfusion for gastrointestinal bleeding: a systematic review and meta-analysis of randomised controlled trials. Lancet Gastroenterol Hepatol. 2017;2(5):354-60. https://doi.org/10.1016/S2468-1253(17)30054-7.
- Robinson GRN, Breedt A, Oghenetega CON, Chetty S. Does pumping iron bring gains? A review of the role of intravenous iron in perioperative blood management. South Afr J Anaesth Analg. 2024;30(1):25-31. https://doi. org/10.36303/SAJAA.3013.
- Sinclair RCF, Bowman MJA, Moppett IK, Gillies MA. Perioperative intravenous iron to treat patients with fractured hip surgery: a systematic review and meta-analysis. Health Sci Rep. 2022;5(3):e633. https://doi.org/10.1002/hsr2.633.
- Low WX, Friend H, Dulleston J, et al. Outcomes of perioperative intravenous iron infusion in femoral fracture surgery: a systematic review and meta-analysis of randomised controlled trials. Surgeon. 2024;22(5):e171-80. https://doi. org/10.1016/j.surge.2024.07.005.
- Meyer J, Cirocchi R, Di Saverio S, et al. Pre-operative iron increases haemoglobin concentration before abdominal surgery: a systematic review and meta-analysis of randomized controlled trials. Sci Rep. 2022;12(2158). https://doi.org/10.1038/ s41598-022-05283-y.
- Liu H-M, Tang X-S, Yu H, Yu H. The efficacy of intravenous iron for treatment of anemia before cardiac surgery: an updated systematic review and meta-analysis with trial sequential analysis. J Cardiothorac Surg. 2023;18(16). https://doi. org/10.1186/s13019-023-02119-2.

