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Peri-operative correction of non-anaemic iron deficiency

Muñoz and colleagues recently published their consensus statement on peri-operative management of anaemia and iron deficiency, an important contribution that will assist clinicians who manage this problem on a daily basis [1]. The authors aim to make "*best-practice and evidence-based statements to advise on patient care with respect to anaemia and iron deficiency in the peri-operative period*". When evaluating such a document, several factors need to be considered, including the strength and generalisability of the evidence underlying the recommendations, and whether safety has been adequately addressed.

Whilst the consensus statement makes several recommendations that appear to be supported by evidence (in keeping with the stated aim of "*improving outcomes in a cost-effective manner*"), others do not. This is particularly true of the recommendation that corrective treatment be initiated for patients with non-anaemic iron deficiency at high risk of developing severe postoperative anaemia. In one of only two studies cited in support, the participants did not meet diagnostic criteria for iron deficiency (mean serum ferritin 113.4 $ng.ml^{-1}$, mean transferrin saturation 25.8%) [2], and in the other, iron status was not determined at all [3]. Furthermore, limited guidance is provided to the reader regarding the appropriate severity of non-anaemic iron deficiency at which to initiate replacement therapy, beyond a reference to a transferrin saturation of less than 20%. This is in conflict with existing evidence-based guidelines that address this condition [4]. Notwithstanding these other recommendations, whilst an improvement in patient-centered outcomes through correction of non-anaemic iron deficiency is certainly biologically plausible, we believe that there is currently insufficient data to recommend routine peri-operative iron therapy for patients with this condition.

With respect to safety, additional published evidence on the association between iron and infection warrants consideration. Although not explicitly the population of interest, studies examining widespread population interventions in the developing world have

demonstrated a strong association between iron supplementation and increased infection [5]. Whilst the meta-analysis cited in the consensus statement suggested no significant increase in infection with intravenous iron, the point estimate favoured increased risk, the confidence interval was wide, and was unable to exclude clinically important differences (RR 1.17; 95%CI: 0.83 to 1.65) [6]. One of us (EL) published a separate meta-analysis (not referenced in the consensus statement), finding a significant increase in infection risk with intravenous iron therapy in hospital inpatients (RR 1.33; 95%CI: 1.10 to 1.64) [7]. Irrespective of these differences, a substantial proportion of relevant randomised controlled trials of iron therapy have not examined infection and/or have been under-powered for this and other patient-centred outcomes, limiting definitive conclusions regarding this important aspect of safety in many peri-operative settings.

Due to this lack of good-quality data regarding benefit and safety, we urge caution when considering iron therapy, particularly intravenous iron, for patients with non-anaemic iron deficiency, until the results of appropriately designed trials are available.

L. F. Miles
D. A. Story
Austin Health,
Melbourne, Australia.
E. Litton
Fiona Stanley Hospital,
Perth, Australia.
*Email: l*achlan.miles@gmail.com

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