IV iron replacement

Dear Editor

The report by Naim and Hunter[1] (*AFP* November 2010) is valuable for drawing attention to the underdiagnosis of iron deficiency causing symptoms. However, it seems to dismiss the risks involved in intravenous iron polymaltose (IVIPM) therapy too readily.

Published trials report varying rates of severe reactions, so by definition the literature is equivocal on this point. Three hundred and fourteen reports of adverse reactions have been made to the Therapeutic Goods Administration (formerly to ADRAC).[2] In 174 cases, the reporting clinician was certain that the reaction was caused by iron polymaltose. The overwhelming majority of these involved anaphylactic symptoms and were treated with antihistamines and steroids after cessation of the infusion.

Drs Naim and Hunter are wrong when they say their study confirmed that 'rates of anaphylaxis are rare'. No episodes occurring in 43 patients gives a 95% confidence interval for the rate of episodes of 0 to 6.7%.

Drs Naim and Hunter seem to imply that IVIPM is sufficiently safe that its use should be broadened to include patients with the mildest degree of iron deficiency who wish to avoid the side effects of oral iron or want a quicker recovery. There is no mention of anaemia.

The origin of the study's criterion of ferritin <= 40 mcg/L for iron deficiency is not clear. The usual criterion for mild iron deficiency is <=15 mcg/L.[3,4]

A trial of oral medication is said to be recommended for mild iron deficiency by the Australian Iron Status Advisory Panel.[4] Choosing therapy with significant risks, over one with mild side effects that takes time to work, may not be the best course of action.

In a sense, it may be true that 'general practitioners can safely use this method... in the primary care setting'. That is, it may be as safe as administration in hospital. However, published evidence does not suggest that IVIPM is an equally safe alternative to oral medication, so its use is probably inappropriate for mild iron deficiency, especially when the ferritin is above 15 mcg/L.

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References

1. Naim M, Hunter J. Intravenous iron replacement: management in general practice. Aust Fam Physician 2010;39:839–41.
2. Office of Product Review, TGA. Available at www.adr.reports@tga.gov.au.
3. Goddard AF, James MW, McIntyre AS, Scott BB, on behalf of the British Society of Gastroenterology. Guidelines for the management of iron deficiency anaemia. May 2005.
4. Patterson AJ, Brown WJ, Roberts DC, Seldon MR. Dietary treatment of iron deficiency in women of childbearing age. Am J Clin Nutr 2001;74:650–6.

Reply

Dear Editor

We appreciate Dr Chaffey's reply and his extensive and thoughtful review.

We would like to clarify that at no stage did we intend to give the impression that IV iron was safer than oral (or potentially intramuscular) replacement therapy. We believe IV therapy is the last line of therapy, where oral treatment or intramuscular iron has failed or is inappropriate.

We acknowledge that we reported a small sample size, so we can't accurately extrapolate from that the incidence of anaphylaxis. What we did comment on were the other side effects that were frequent enough in our small sample size. Nevertheless, from the Therapeutic Goods Administration report[1] on side effects to iron polymaltose, it is very difficult to make sense of the reports, given that there is no information on the dose given, the rate of infusion, or the method of administration (IM or IV). There are a number of anaphylactoid reactions reported, but less than 20 seem to be true-type one anaphylactic reactions (with skin reactions, airway problems and hypotension). Haines et al[2] gave the highest reported figures for adverse reactions that we could find in the literature, but even they state that they would still administer the product. We based our discussion of safety on the available literature. Certainly if there was serious risk of anaphylaxis, we don't believe it would still be used as widely as it is, intravenously.

We disagree with Dr Chaffey when he states that these patients were 'not iron deficient by the usual criterion' – or that 'mild iron deficiency is a ferritin <15 mcg/L'. According to all reasonable authorities, including those who have studied bone marrow to assess iron stores, figures of <40 mcg/L probably indicate severe iron deficiency, and certainly <15 mcg/L would indicate iron depletion. Dr Steve Flecknoe-Brown, haematologist, in 'The Transfusion Question'[3] gives a detailed view of his experience with IVIPM use over a 20 year period. First he describes a ferritin of <20 mcg/L as iron depletion, not iron deficiency. We know that reference ranges for ferritin include measuring it in an iron-depleted community, and there is strong evidence that levels <40 mcg/L, as we stated, are states of iron deficiency. He describes the amount of iron polymaltose needed to give as a total dose replacement (around 10–15 ampoules). This is far in excess of what we use. Flecknoe-Brown and colleagues all consider the product quite safe and include papers and independent surveys that have been done on their patients to support this.

We believe that in situations where a patient is unwell or at risk because of iron deficiency (they don't have to be anaemic), where oral products or intramuscular iron can't be used, careful use of IVIPM is warranted and safe. We use a small dose (nowhere near the total loading dose), given slowly, and have found it a very useful addition to our therapeutic toolbox.

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References

1. Office of Product Review, TGA. Available at www.adr.reports@tga.gov.au.
2. Haines ML, Gibson PR. Delayed adverse reactions to total-dose intravenous iron polymaltose. Intern Med J 2009;39:252–5.
3. Available at www.thetransfusionquestion.com.au/Debate4.aspx.

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