Iron infusion and newer intravenous iron formulations

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To the Editor: Iron deficiency (ID) and ID anemia (IDA) are common health problems worldwide. The World Health Organization (2011) estimated that 34% of the global population (>2 billion) is affected by anemia and that the most common type was ID (50% of total anemia), which primarily affects women of reproductive age.[1] Although intravenous (IV) iron has been used to treat ID and IDA for more than six decades, its use in primary care settings has been infrequent compared with its use in tertiary centers due to the historical concern of anaphylaxis, among others. The newer (non-dextran) IV formulations, which allow complete or near-complete replacement in a single sitting of 15 to 30 min, have an improved safety profile, and better tolerability, efficacy, and effectiveness compared with oral iron therapy. They are suited for administration in the primary care or community practices in a proper setting. Although oral iron remains the first-line therapy for iron replacement in most guidelines, its common side effects of gastric upset and constipation, and the need to take it regularly for months to replenish iron stores, often result in non-adherence. Intramuscular iron injection is no longer favorable because of pain, skin discoloration and requirement of multiple injections.

Although ID and IDA symptoms, such as fatigue, tiredness, and dizziness, are non-specific, the untreated condition can eventually affect cognition, academic achievement, exercise tolerance, work productivity, and quality of life. Indications for iron infusion include ID and IDA caused by the underlying conditions such as malabsorption, deficient diet, excess blood loss, faster body growth, chronic diseases[2] and intolerance to oral iron as detailed in Supplementary Annexure 1, http://links.lww.com/CM9/A566. Contraindications for infusion are anemia not caused by ID; known anaphylaxis to the specific iron product, iron overload conditions, and high-risk patients with serious comorbidities [Supplementary Annexure 1, http://links.lww.com/CM9/A566]. Precautions include individuals with acute infection, asthma, marked atopy, liver dysfunction, or conditions associated with low phosphate in the body. The detail of investigation for ID and IDA is beyond the scope of this article, and it is always important to address the underlying etiology while providing the replacement.

In terms of benefits, IV iron rapidly restores iron and expedites hemoglobin synthesis. Newer non-dextran formulations, such as ferric carboxymaltose (FCM), ferric derisomaltose (FDM), iron sucrose (ISC), and ferumoxytol (FOT) contain carbohydrate cores that bind elemental iron more tightly, allowing much slower release with marginal or fewer reactions.[3] They have also demonstrated greater efficacy and effectiveness in improving the quality of life and productivity compared with oral therapy and earlier parenteral formulations.[4,5] Newer formulations may also reduce health costs by lessening visits to hospitals and healthcare providers.[5] Some studies have indicated that the newer generations of IV iron are underutilized due to fears about anaphylactic reactions, but these reactions were far more common compared with high molecular weight iron dextrans (e.g., imferon, dexferrum), which are no longer available.[3,6] Certain reviews suggested reconsidering the current paradigm whereby oral iron treatment is considered a first-line therapy, but it needs a broad consensus with further evaluation.[3,6,7] More than 20 randomized studies revealed that IV administration of iron offers better tolerability, efficacy, and effectiveness than oral iron therapy.[8,9] One randomized control trial reported that the cost of IV use does not exceed that of oral therapy, whereas IV use is more beneficial in terms of superior tolerance and effectiveness.[10] The adverse effects of iron infusion are major anaphylactic (rare), and less severe or minor reactions such as urticaria, dizziness, facial flushing, arthralgia, myalgia, dysgeusia etc. as explained in Supplementary Annexure 2 [http://links.lww.com/CM9/A566].[11,12]

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Regarding parenteral iron dosage, the Ganzoni formula can usefully estimate the replacement dosage. However, a simplified calculation method based on the current hemoglobin level and body weight can also be used [Supplementary Annexure 3, http://links.lww.com/CM9/A566]. Each iron product has specific instructions for dilution and duration of infusion, and specific product instructions or local guidelines should be referred to if available. Generally, FCM (1000 mg) and FDM (1000–1500 mg) can be given as a single dose over 15 to 30 min. As per manufacturers, 510 mg of FOT is to be given at a time, but trials of 1020 mg infusion over 15 to 30 min reported no safety concerns, which needs further evaluation.[13] ISC requires multiple fraction doses of a maximum of 100 to 200 mg at a time and is commonly used for renal dialysis patients. Iron dextran (even low molecular weight) and iron polymaltose usually require a test dose with longer infusion duration. The preparation and administration of IV iron and ways to avoid or minimize undesirable effects are described in Supplementary Annexure 4, http://links.lww.com/CM9/A566.

Head-to head comparisons of the four non-dextran formulations (FCM, FDM, ISC, and FOT) in the literature yielded comparable or near-equal efficacy and safety profiles overall [see Supplementary Digital Content, Annexure 5, http://links.lww.com/CM9/A566 for further references].[14-16]

Overall, little current evidence recommends a single best iron product for infusion among these four. Certainly, iron infusion with those formulations has a better safety profile than dextran iron and provides a more convenient, effective alternative to adhering to months of oral iron replacement. Formulations that can deliver the replacement with a single large dose would attract more utilization from the aspects of convenience and less frequent visits to healthcare providers. Although anaphylactic reactions are rare with newer formulations, close monitoring during administration is recommended for infusion with all IV iron products. Choice of iron product will largely be determined by local availability/guidelines, cost, and convenience.

Conflicts of interest

None.

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