IRON CORNER

IV Iron and Erythropoietic Stimulating Agents (ESAs)

Background

Iron is an essential component in hematopoiesis and, as such, should supplement ESA treatment. In 1989, the introduction of ESAs led to a renewed interest in parenteral iron therapy. After initiation of ESA therapy, functional iron deficiency occurred in almost every patient as the result of the non-physiologic administration of ESA.[1]

By 1997, reports showed that maintaining serum ferritin and percent transferrin saturation levels above 100 ng/mL and 20% resulted in reaching and maintaining better target Hb levels and/or lowering the dose of ESA required. Oral iron was used initially, but it was poorly tolerated and only marginally effective, so IV iron was employed to treat these patients. Virtually all hemodialysis patients receiving ESA should be treated with IV iron.

Usage

ESA treatment alone will rapidly deplete iron stores leading to functional iron deficiency and the production of iron-poor RBCs (iron-deficient erythropoiesis).

- In most cases, patients receiving erythropoietin therapy are unable to keep up with via oral iron, the demand for iron and intravenous iron is indicated.

- The large majority of hemodialysis patients will require intravenous iron supplementation. Oral ferric citrate or dialysate iron in the form of ferric pyrophosphate citrate (FPC) may be an effective alternative in some hemodialysis patients.[2]

When administered with ESAs, IV iron prevents both absolute and functional iron deficiency and serves to minimize the dose of ESA needed to achieve target range Hb level.

- Evidence from multiple studies in CKD patients conducted since 1992 shows that intensive IV iron supplementation allows a reduction in EPO dose of 19% to 70%. A recent randomized controlled trial of intravenous iron in patients undergoing maintenance hemodialysis (the PIVOTAL Trial) showed that high dose IV iron administered proactively to an upper safety threshold of transferrin saturation of < 40% and a ferritin < 700 ng/mL, compared to lower dose iron administered reactively to maintain a transferrin saturation > 20% and a ferritin > 200 ng/mL, resulted in fewer blood transfusions, faster increase in the hemoglobin level and reduced doses of ESAs. High dose iron also appeared to protect against hospitalization for heart failure.[3]

- Nine studies in chemotherapy induced anemia have shown a clear benefit from the addition of IV, and not oral, iron to ESA therapy with only one, clinical trial showing no benefit (Steensma, ASH 2009). In the nine studies showing benefit, the common denominators were improved hemoglobin response, shortened time to target hemoglobin, and decreased ESA usage for the same benefit.

Reimbursement Issues with IV Iron and ESA Administration

Under the current Committees for Medicare and Medicaid Services (CMS) Coverage Determinations governing usage of ESA, if iron deficiency is present, ESAs are contraindicated until iron repletion has been accomplished.

The conundrum is that there is no ICD10 code for either functional iron deficiency or iron-restricted erythropoiesis, which for all intents and purposes is the same thing. Clearly, the lack of codes for functional iron deficiency creates a problem in hematology and oncology practices where these drugs are widely used in that they may limit reimbursement for both ESAs and intravenous iron.

The current guidance from CMS restrict payment if ESA and IV iron is given on the same day. Although inexplicable at first, as this regulation clearly increases the number of office visits outside of dialysis centers, where the regulation does not apply, given the requirement for iron repletion prior

to ESA usage, if Iron deficiency anemia, unspecified (D50. 9) is placed on a billing form, the ESA will not be paid for. On the other hand, if (D50. 9) is not placed on the billing form, the IV iron will not be reimbursed. Providers are urged to consult with billing and coding professionals within their institution as well as their regional Medicare Administrative Contractor. Single dose intravenous iron replacement with 1 gram of iron based on an transferrin saturation less than 20% at the time of an initial or subsequent visit may be the most practical course of action to both appropriately mange clinical care for the patient and optimize coverage and reimbursement.

References

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