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.

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. Currently, virtually all hemodialysis patients receiving ESA are 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.

- In many cases, patients receiving erythropoietin therapy are unable to keep up with iron losses via oral iron, and intravenous iron may be indicated.
- Approximately 25% of hemodialysis patients can be maintained on oral iron supplementation, the others require intravenous iron supplementation.

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%
- 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, albeit well done, 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 parlance regulating usage of ESA if iron deficiency is present, ESAs are contraindicated until iron repletion has been accomplished.

The conundrum is that there is no ICD9 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.

The current guidance from the Committees for Medicare and Medicaid Services (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 (280.9) is placed on a billing form the ESA will not be paid for. On the other hand, if 280.9 is not placed on the billing form, the IV iron will not be reimbursed.

References

Shander A, Spence RK, Auerbach M. Can intravenous iron therapy meet the unmet needs created by the new restrictions on erythropoietic stimulating agents? Transfusion. 2010 Mar;50(3):719-32.

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