Chemotherapy-induced anemia at an urban academic medical center: Iron studies and supplementation

Stacy S. Shord and Sandra Cuellar

Objectives: To determine the number of patients with chemotherapy-induced anemia receiving an erythropoiesis-stimulating agent (ESA) in whom iron studies were completed and iron supplementation was provided and to document the response rate of ESA therapy without parenteral iron at our medical center.

Design: Retrospective chart review.

Setting: Urban (Chicago) academic medical center between January 2004 and December 2005.

Patients: Ambulatory patients with a nonmyeloid malignancy receiving chemotherapy during a 2-year period in whom hemoglobin (Hb) was less than 11 grams/dL or ESA therapy was documented.

Intervention: Review of medical records.

Main outcome measures: Number of patients reaching target Hb, time to reach target Hb, number of patients receiving a transfusion, number of patients with iron studies, and number of patients receiving iron supplementation.

Results: A total of 174 medical records were reviewed, and 50 patients met study criteria. Of these, 38 patients were treated with darbepoetin alfa, 11 patients were treated with epoetin alfa, and 1 patient was not treated with either agent. 20 patients achieved the target Hb level of 12 grams/dL within a median of 7 weeks (range 1–24 weeks). Only five patients treated with an ESA received iron supplementation, one responder and four nonresponders. Iron indices were measured in 20 patients (40%); 14 patients were candidates for iron therapy based on transferrin saturation, and 3 of these 14 patients received oral iron supplementation. Six responders and six nonresponders received a transfusion (25%).

Conclusion: The overall response rate and time to Hb response were consistent with previous reports. Iron indices were not commonly measured before ESA therapy was started, and only a few patients were provided oral iron supplementation at our medical center.

Keywords: Anemias, chemotherapy, iron, nutritional supplements, erythropoiesis-stimulating agents.

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About 30% to 90% of patients diagnosed with cancer develop anemia associated with the disease or the treatment,[1,2] and serious or life-threatening anemia develops in up to 80% of patients diagnosed with lymphomas or solid tumors.[3] The World Health Organization defines anemia as hemoglobin (Hb) less than 12 grams/dL in women and less than 13 grams/dL in men.

A recombinant form of the hormone erythropoietin was first introduced in 1991 as an alternative to transfusions to manage anemia in patients with nonmyeloid malignancies receiving chemotherapy.[4] Today, epoetin alfa and darbepoetin alfa are commonly prescribed to decrease the need for red blood cell transfusions. Multiple clinical studies indicate that epoetin alfa and darbepoetin alfa produce significant increases in Hb levels, significant decreases in transfusions, and substantial improvements of quality of life,[5–9] with several head-to-head comparisons indicating that these agents provide similar outcomes.[10–13]

At a Glance

Synopsis: Patients commonly received erythropoiesis-stimulating agent (ESA) therapy without sufficient iron availability or supplementation, according to this analysis of 50 patients with a nonmyeloid malignancy who were receiving chemotherapy and had hemoglobin (Hb) levels of less than 11 grams/dL. Iron indices were measured in just 20 patients, 14 of whom were candidates for iron therapy; 11 of these 14 patients received no iron supplementation, despite their established need, and the three treated patients received oral iron, a relatively ineffective formulation in this population.

Analysis: *Parenteral iron therapy improves Hb response to ESAs, lowers the dose of ESA needed to reach target Hb, improves patient quality of life, and reduces the need for transfusions. Parenteral iron combined with ESA therapy also can result in cost savings (estimated at $100/patient/week in one study). The advantages of combining ESA therapy with parenteral iron prompted these authors to develop clinical practice guidelines to assess iron indices in all patients with cancer- or treatment-related anemia and to administer parenteral iron with ESAs in patients with functional iron deficiency. The guidelines are in line with a Centers for Medicare & Medicaid Services memorandum regarding the initiation and maintenance of ESAs in patients with cancer- or treatment-related anemia. Collectively, these findings support the need to obtain iron studies before starting ESAs and that parenteral iron should be considered in the presence of iron-restricted erythropoiesis.*

However, these studies indicate that up to 50% of patients fail to demonstrate a response to these agents after a minimum of 12 weeks of treatment.[5–9] Why these agents fail to promote a clinically meaningful response in some patients is unclear. Some patients with cancer are thought to develop iron-restricted erythropoiesis (i.e., functional iron deficiency or acquired iron insufficiency syndrome); this occurs when the reticuloendothelial system cannot release stored iron quickly enough to permit the incorporation of iron into Hb during erythropoiesis despite adequate iron stores.[14] In contrast, absolute iron deficiency occurs with acute blood loss or impaired iron absorption with a measurable decrease in serum and stored iron. About 13% of patients with cancer- or treatment-related anemia are estimated to have absolute iron deficiency, and about 46% of patients have functional iron deficiency.[15] Of note, erythropoiesis-stimulating agents (ESAs) may worsen functional iron deficiency by accelerating erythropoiesis and increasing the demand for iron. Six recent studies demonstrated that parenteral iron improves the response rate associated with ESAs, as reflected by a greater increase in baseline Hb (intravenous [I.V.] iron 68–93% versus oral or no iron 25–73%) and a shortened time to reach target Hb.[16–21] These studies suggest that a possible synergy exists between parenteral iron and ESA therapy, that iron indices should be measured in all patients with cancer- or treatment-related anemia, and that parenteral iron should be administered with ESAs to maximize their effectiveness, especially in light of the recent scrutiny of ESA therapy for patients with cancer- or treatment-related anemia.[22]

Objectives

The observed synergy between ESA therapy and parenteral iron prompted us to examine the management of anemia in patients with cancer at an urban academic medical center. The objectives of this study were to determine the number of patients with cancer receiving ESAs in whom iron studies were completed and iron supplementation was provided and to document the response rate of ESA therapy without parenteral iron at our medical center. Our findings prompted us to develop recommendations for assessing iron indices in all patients with cancer- or treatment-related anemia and for administering parenteral iron with ESA therapy at our medical center. Of note, this study was conducted before issuance of a Centers for Medicare & Medicaid Services (CMS) memorandum regarding use of ESAs in patients with cancer.[22]

Methods

The first 50 ambulatory patients who met the below inclusion criteria were admitted to the study. This was a multicenter study completed as part of a study (Anemia Insights) sponsored by Amgen. The data described in the current work are from our medical center. The University of Illinois at Chicago Cancer Center Protocol Review Committee and Institutional Review Board approved the study.