Once-Weekly Dosing of Epoetin-α Increases Hemoglobin and Improves Quality of Life in Anemic Cancer Patients Receiving Radiation Therapy Either Concomitantly or Sequentially with Chemotherapy

Authors: Shasha D, George MJ, Harrison LB
Source: *Cancer*, 2003;98:1072-9

Background

- Anemia is very common in cancer patients, whether it results from radiation therapy, chemotherapy, or the disease itself
- Anemia often causes the symptom of fatigue with associated functional impairment and decrease in quality of life
- Anemia also can cause a decrease in oxygen delivery to the tumor, which could result in lower cure (especially with radiation therapy)
- Previously, patients with severe anemia required red blood cell transfusions, with associated complications
- Recently, several studies have indicated the efficacy of weekly recombinant human erythropoietin (epoetin-α) in increasing hemoglobin levels during radiation therapy or during chemotherapy
- This study reports on the effectiveness and safety of weekly epoetin-α in the treatment of anemia in patients with nonmyeloid malignancies who are undergoing chemotherapy and radiation therapy

Materials and Methods

- This was a single arm, nonrandomized study over 16 weeks of 777 patients
- Patients were required to have anemia (as defined as hemoglobin < 11 g/dl) and receiving radiation therapy either concurrently or sequentially with chemotherapy
- Patients were required to have received at least 40 Gy within the past 8 weeks and/or a course of radiation therapy lasting > 4 weeks during the 16 week study period
- Patients received 40,000 units of epoetin-α subcutaneously weekly. If hemoglobin increased < 1 g/dl after 4 weeks, the dose was increased to 60,000 units
- Epoetin-α was discontinued if the hemoglobin reached > 13 g/dl and decreased if the rise was > 1.3 g/dl in any given week
- Primary endpoint was hematologic response, defined as an increase of hemoglobin of > 2 g/dl or the achievement of a hemoglobin level of > 12 g/dl at any point during the study
- Number of transfusions required as well as quality of life scores (as obtained by survey) were also measured

Results

- 442 patients were evaluable for hematologic response
- Mean pretreatment hemoglobin level for evaluable patients was 9.9 g/dl
- There was a significant increase in the mean hemoglobin level from baseline to time of final evaluation of 1.9 g/dl
- Mean final hemoglobin level was 11.8 g/dl
- The overall response rate (to 40,000 units or 60,000 units) was 74%
- A total of 35% of patients required an increase to 60,000 units
- 10% of patients were transfused in the 6 months prior to study compared to 4.9% during the study
- 359 patients filled out the questionnaire measuring quality of life
- Final scores of quality of life demonstrated statistically significant improvements from baseline
- Adverse events were similar to those commonly reported by patients receiving chemotherapy and radiation therapy

Authors' Conclusions

- Weekly epoetin-α was found to significantly increase hemoglobin levels in patients receiving chemotherapy and radiation therapy
- This increase was regardless of dose and type of radiation therapy, chemotherapy, or tumor response
- This had an associated decrease in the percentage of patients requiring transfusions
- The increase in hemoglobin levels also improved the quality of life in these patients

Scientific Implications

Patients undergoing treatment for cancer with radiation therapy and chemotherapy often have anemia. This can cause profound fatigue with associated decreased quality of life, as pointed out by the authors. Anemia has also been shown to decrease cure rate in cervical and head and neck tumors. Therefore, it is imperative that anemia, especially severe anemia, be rectified. This study demonstrates that weekly epoetin-α can be used safely and efficaciously in this regard. However, this was a single arm, nonrandomized study in which several hundred of the patients were not evaluable for hemoglobin response or quality of life. Most were dropped because they did not meet the minimum radiation requirements, though this still could have skewed the data. Seventy four per cent of patients had a response to epoetin-α as measured by a 2 g/dl increase or a hemoglobin of > 12 g/dl with associated decrease in transfusion requirement and increase in quality of life. However, these parameters could be achieved at any point during the study, which was up to 16 weeks. Therefore, though the efficacy was high, its onset could have also been very slow. This is a large disadvantage in patient symptom relief and especially cancer treatment efficacy. Another aspect of the study not reported is cost. Epoetin-α is an expensive medication, especially if achieving efficacy means increasing the dose to 60,000 units per week. This should also be considered before initiating therapy. Therefore, although epoetin-α is efficacious and safe, it is often also slow in onset with a high expense. Transfusions increase the hemoglobin immediately and may be better in some patients. However, this increase in hemoglobin with transfusion may be short-lived. In addition, blood bank resources are finite, there is always the risk of infection or immunosuppression, and there is a cost associated with transfusion as well. Therefore, weekly administration of epoetin-α is a good alternative to transfusion, as long as the disadvantages are considered.