

**EVALUATION OF STRATEGIES TO IMPROVE THE APPROPRIATE
USE OF ERYTHROPOIETIC AGENTS
IN ANEMIC PATIENTS IN THE LONG TERM CARE FACILITY**

A Pharmacy Practice Paper

Peggy Jones, RPh

**University of Florida
College of Pharmacy
Working Professional Doctor of Pharmacy**

EVALUATION OF STRATEGIES TO IMPROVE THE APPROPRIATE USE OF ERYTHROPOIETIC AGENTS IN ANEMIC PATIENTS IN THE LONG TERM CARE FACILITY

A Pharmacy Practice Paper
Peggy Jones, RPh

Background:

Anemia is a frequent problem among the elderly. A recent study estimated the prevalence of anemia (hemoglobin <12 g/dL for women and < 13 g/dL for men), at 32 to 64% chronic skilled-nursing facility subjects. (1) Erythropoietic agents such as epoetin alfa and darbepoetin alfa improve morbidity and mortality and are approved for treating patients with anemia due to chronic renal failure, zidovudine treated HIV patients, and cancer patients treated with chemotherapy. (2,3,4) Epoetin alfa was recently approved for use in anemic patients (hemoglobin >10 or ≤13 g/dL) scheduled to undergo elective, noncardiac, nonvascular surgery to reduce the need for allogeneic blood transfusions. (3) Anemia is often a concomitant diagnosis in patients with heart failure (HF) and worsens the HF prognosis. (5,6) One study suggests that erythropoietin should be a part of congestive heart failure management. (7)

The cost of using erythropoietic agents in the long term care (LTC) facility has put considerable burden on the medication budget. Efforts to minimize the cost of these medications while at the same time maximize the outcome has become a focus for the nursing facility administrator. LTC pharmacy service providers may be able to play an important part in initiating anemia protocols.

The purpose of this paper is to review the literature for pharmacist intervention in anemia management with erythropoietic agents and to examine anemia management efforts at one LTC provider pharmacy. Based on the evaluation, changes for improvement in services were implemented.

Evaluation of Practice Guidelines:

Published clinical practice guidelines for anemia management are available from the National Kidney Foundation's Dialysis Outcomes Quality Initiative (K-DOQI). (8) The treatment guidelines for the management of anemia in patients with chronic kidney disease (CKD) can be summarized by Figure 1.

The successful use of erythropoietic agents to treat anemia depends on a number of factors. The underlying cause for the anemia should be evaluated. Artz, et. al., examined the mechanisms of unexplained anemia in 60 nursing home residents. (9) Iron deficiency was found in 23% of the patients. 45% of the anemic residents fit the description of idiopathic anemia. The authors found that the patients with idiopathic anemia had a blunted endogenous erythropoietin response. Anemia due to chronic renal insufficiency was found in 10% of the patients and anemia of chronic disease found in 13% of the patients.

Erythropoietic agents are not indicated for anemia due to iron or folate deficiencies, hemolysis or gastrointestinal bleeding. Prior to initiation of therapy with either epoetin alfa or darbepoetin alfa, the patient's CBC and iron stores should be evaluated. (8) Transferrin saturation should be at least 20% and serum ferritin at least 100 mcg/L. Blood pressure should be adequately controlled and closely monitored during therapy. Medication profiles should be reviewed for medications that may contribute to blood loss and anemia, specifically the use of NSAIDS or warfarin.

Evaluation of Strategies to Improve the Use of Erythropoietic Agents:

To, et. al., compared the effectiveness of a pharmacist-implemented anemia management protocol in an outpatient hemodialysis unit with that of a physician-based management protocol. (10) Forty-nine patients were followed for a total of six months, the first three months by physician and the last three months by a pharmacist. Pharmacists had prescriptive authority as defined by the protocol and could make changes in epoetin alfa and iron therapies. The authors concluded that the pharmacist management of anemia in hemodialysis patients under protocol was as effective as physician management. Hematocrit was the primary outcome variable used for this assessment. Secondly, there was an overall reduction in the amount of epoetin alfa used in the pharmacist managed group, though this was not statistically significant. The pharmacist managed group used more IV iron to achieve the necessary TSAT levels and ferritin concentrations to meet protocol standards.

A structured team approach to anemia management in nineteen erythropoietin resistant dialysis patients was studied by Dar Santos, et. al. (11) They used the same team of two pharmacists and a nephrologist to follow 19 patients refractory to epoetin alfa therapy. These patients were on > 300 units/kg/wk doses of epoetin alfa and had mean hemoglobin levels of 10.38 ± 1.25 g/dL. The team evaluated the patients for contributing causes of anemia (iron deficiency, dysfunctional vascular access, hyperparathyroidism, inadequate dialysis, blood loss, bone marrow suppression) and reversed these causes wherever possible. Within 8 months the team was able to reduce the dose of epoetin alfa and increase mean hemoglobin levels to 11.59 ± 1.5 g/dL. A significant cost savings of \$45,007 (Canadian) was realized from the intervention.

Brimble, et. al. evaluated a protocol approach vs. a non-protocol approach to anemia management in hemodialysis patients. (12) In this study, 215 patients were randomized to either usual care or a protocol approach to anemia management with epoetin alfa. They observed that while both groups achieved the target hemoglobin of 11 to 12.5 g/dL, overall doses of epoetin alfa were reduced for patients enrolled greater than 5 months in the protocol group. Based on this data, the authors estimated that the reduction in epoetin alfa dose would be associated with a cost savings of \$1245.98 per patient per year (based on a \$0.0086 per unit) and that in their study center of >430 hemodialysis patients, an annual savings of >\$535,000 would be realized.

Practice Implementation:

Initially when approached by several administrators of the LTC facilities, the provider pharmacy ran prescription reports weekly to determine which patients had received epoetin alfa or darbepoetin alfa. CBC results were then reviewed via the internet from the laboratory services provider for these patients. A pharmacist reviewed the

hemoglobin and hematocrit to determine if the patient was within the established goal hemoglobin and/or hematocrit range. A report was sent via facsimile to the director of nurses at the long term facility with a recommendation to either continue to monitor the use of the erythropoietic agent or re-evaluate the dosage and/or need for the erythropoietic agent.

This service provided the director of nursing with a list of patients receiving erythropoietic agents and their current hemoglobin and hematocrit status.

Several areas for improvement were identified. First of all, a method to follow trends in the hemoglobin and hematocrit over time and examine other CBC indices for cause of anemia was needed. Secondly, patient profiles needed to be reviewed for diagnosis, supplemental iron therapy, medications that may be contraindicated or worsen anemia, concurrent diagnosis that may signal inappropriate use of erythropoietic agents (i.e., anemia due to acute blood loss). A protocol was established through the company's Medical Advisory Board using darbepoetin alfa (Aranesp®) as the preferred formulary product. (see Figure 2.) Lastly, a method for communication was needed for recommendation implementation and follow up.

Practice Experience:

To address the identified areas for improvement, laboratory profiles were accessed online and a cumulative CBC report printed, allowing for a review of the indices over time. In addition, iron studies, cumulative chemistry panels, drug levels, PT/INR were also printed. Each week when the erythropoietin usage report was run, complete computerized patient profiles were printed for each patient. These profiles include the patient's drug orders, diet orders, treatment orders, diagnosis, date of birth, date of admission and physician name.

The patient laboratory report was attached to the patient profile. The reports were then reviewed by the clinical pharmacist for patient diagnosis, patient renal function status (as determined by the MDRD abbreviated formula for assessing glomerular filtration rate), iron supplementation, and medications that may indicate gastrointestinal blood loss. A report was then typed up and faxed to the facility director of nurses. Follow up phone calls to make sure the report had been received by the facility nursing director were made.

Several problems with therapy were discovered during the reviews. None of the patients had orders to evaluate iron stores. Often patients did not have CBCs monitored as suggested by the protocol. Iron supplementation was either lacking or inadequate as suggested by the protocol. Drug therapy problems also included patients treated with warfarin and INRs above the suggested therapy range of 2 to 3. Many patients had orders for H2 antagonists or proton pump inhibitors without an indication or diagnosis. These drug therapy problems lead to the question of whether the anemia was due to bleeding from anticoagulation or GI blood loss.

Recommendations:

While the focused review of patients who had erythropoietic agents dispensed expanded with the above experience, several more areas are still in need of improvement.

Currently patient weights are not communicated to the pharmacy. This information is necessary to review the profiles for inadequate or excessive doses of erythropoietic agents.

Often there was a significant time lag in the pharmacist recommendation and an order by the prescribing physician, indicating that the method of communication was inadequate. Perhaps prescriptive authority per protocol for iron supplementation and lab studies could have circumvented the delay.

The outcome of the above reviews has not been fully evaluated. Cost data, change in hemoglobin, change in patient functional status, number of hospital admissions, length of sub-acute rehabilitation stay are all areas that could be tracked and measured as outcomes.

Educational needs for the facility staff on anemia management should also be addressed. Communication with the facility's consultant pharmacist may help address issues of follow-up and education.

And finally, a measure of physician acceptance of the anemia management program should be evaluated. A team approach to developing a working protocol for anemia management in the LTC setting should be explored.

Conclusions:

Anemia management and cost containment in the long term care patient is a problem area that needs continual focus and attention. Protocol driven prescribing and monitoring has shown to improve outcomes and/or reduce cost in other practice settings. (8,9) Further study of the nursing home population and their response to erythropoietic agents is needed to determine the cost effectiveness and overall outcome of the use of these agents.

References:

1. Artz AS, Fergusson D, Drinka PJ, Gerald M, Gravenstein S, Lechich A, Silverstone F, Finnigan S, Janowski MC, McCamish MA, Ershler WB. Prevalence of anemia in skilled-nursing home residents. Arch Gerontol Geriatr. 2004 Nov-Dec;39(3):201-6.
2. Epogen (epoetin alfa) package insert, Amgen, Inc., Nov. 2004.
3. Procrit (epoetin alfa) package insert, Ortho Biotech Products, LP. Feb. 2005.
4. Aranesp (darbepoetin alfa) package insert, Amgen, Inc. Mar. 2005.
5. Ezekowitz JA, McAlister FA, Armstrong PW. Anemia is common in heart failure and is associated with poor outcomes. Insights from a cohort of 12,065 patients with new-onset heart failure. Circulation 2003; 107: 223-5.
6. Mozaffarian D, Nye R, Levy WC. Anemia predicts mortality in severe heart failure: the prospective randomized amlodipine survival evaluation (PRAISE). J Am Coll Cardio 2003; 90: 303-8.
7. Silverberg DS, Wexler D, Blum M, Schwartz D, Wollman Y, Iaina A. Erythropoietin should be a part of congestive heart failure management. Kidney Int 2003;64 (suppl 87):S40-7.

8. National Kidney Foundation. K/DOQI clinical practice guidelines for anemia of chronic kidney disease, 2000. *Am J Kidney Dis* 2001;37(suppl 141):S182-238.
9. Artz AS, Ferguson D, Drinka PJ, Gerald M, Bidenbender R, Lechich A, Silverstone F, McCamish MA, Dai J, Kellar E, Ershler WB. Mechanisms of Unexplained Anemia in the Nursing Home. *JAGS* 52:423-427, 2004.
10. To LL, Stoner CP, Stolley SN, Buenviaje JD, Ziegler TW. Effectiveness of a pharmacist-implemented anemia management protocol in an outpatient hemodialysis unit. *Am J Health Syst Pharm* 2001;58:2061-5.
11. Dar Santos AE, Shalansky KF, Jastrzebiski JP. Management of anemia in erythropoietin-resistant hemodialysis patients. *Ann Pharmacother*. 2003 Dec;37(12):1768-73.
12. Brimble KS, Rabbat CG, McKenna P, Lambert K, Carlisle EJ. Protocolized Anemia Management with Erythropoietin in Hemodialysis Patients: A Randomized Controlled Trial. *J Am Soc Nephrol* 14: 2654-2661, 2003.

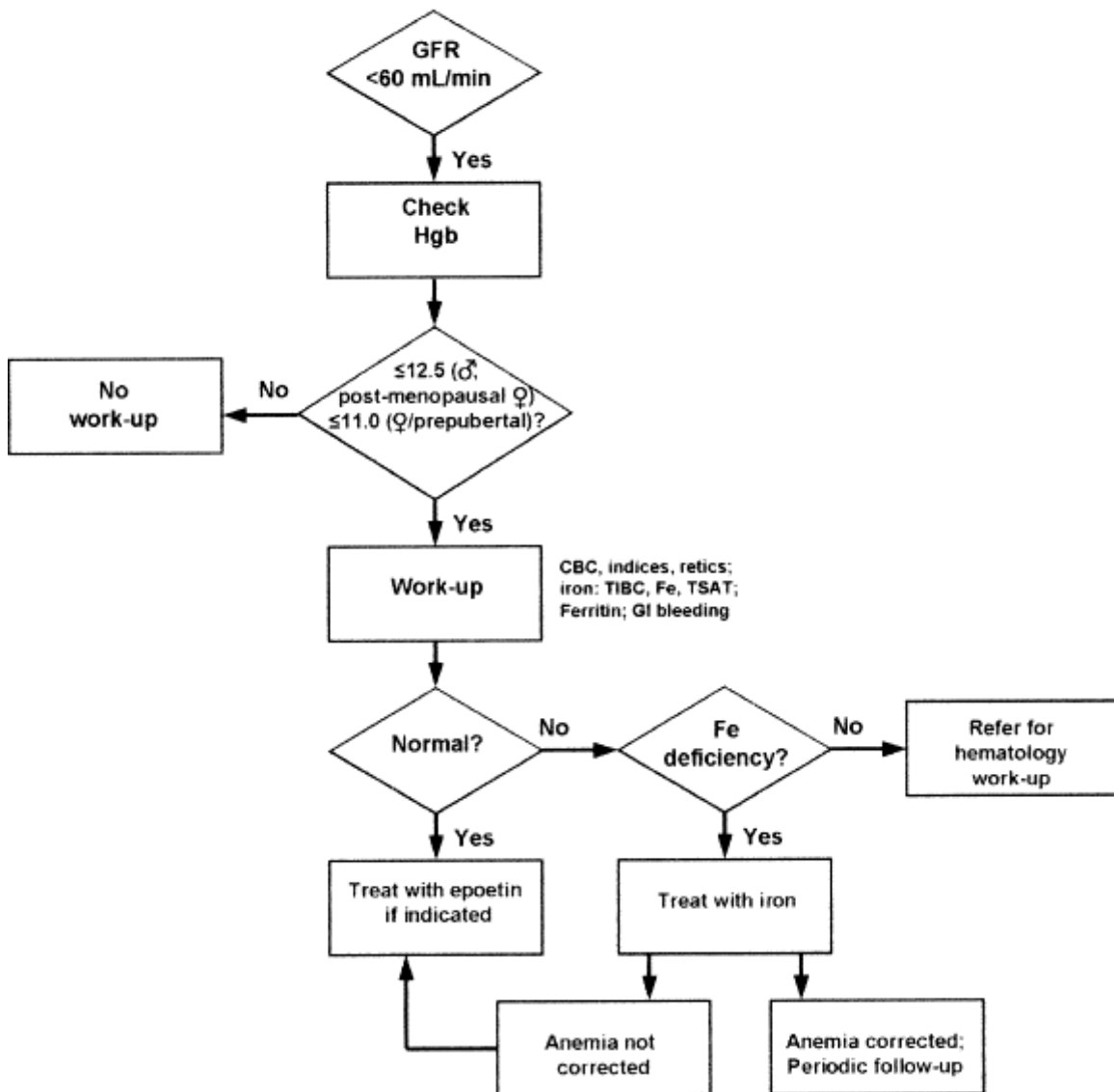


Figure 1

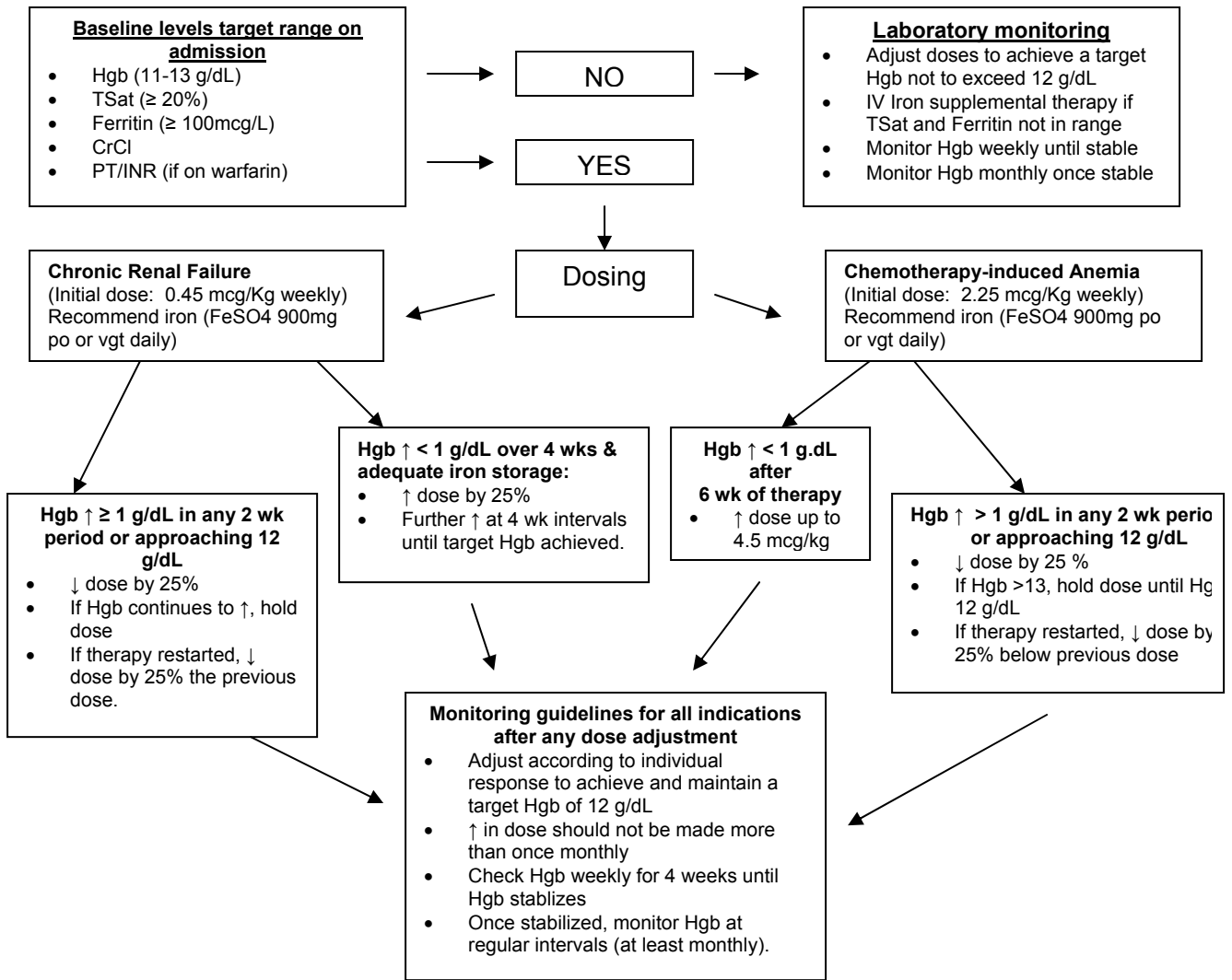


Table 1