Published in final edited form as:
J Am Med Dir Assoc. 2009 July ; 10(6): 436–439. doi:10.1016/j.jamda.2009.03.010.

Assessing the Quality of Prescribing and Monitoring Erythropoiesis Stimulating Agents in the Nursing Home Setting

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Abstract

Introduction—As many as 50% of all nursing home (NH) residents meet the World Health Organization criteria for anemia. The objectives of this study were to determine the prevalence and appropriateness of prescribing and monitoring of erythropoiesis stimulating agents (ESAs) used to treat anemia in the NH setting.

Methods—Cross-sectional, one-month study of all NH residents in four community-based, university-affiliated NHs between January and February 2008. Residents were included in the analysis if they received at least one dose of an ESA during the study duration. Data collected through chart review included basic demographic information, ESA indication, ESA dosage, concurrent administration of iron supplements, hemoglobin (Hgb) monitoring, and blood pressure measurements.

Results—A total of 4.5% (22/485) of NH residents received at least one dose of an ESA. Residents who received ESAs had a mean age of 80.4 (± 14.5) years. Most residents who received ESAs were female (64% [14/22]), white (68% [15/22]), and had a mean weight of 72.0 (± 20.84) kg. Only 27% (6/22) of residents were prescribed an ESA for a FDA-approved indication. Darbepoetin alfa was the most commonly prescribed ESA (64% [14/22]) with a mean weekly dose of 70.8 (± 68.1) mcg, followed by epoetin alfa (37% [8/22]) with a mean weekly dose of 22,625 (± 21,232) units. More

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than one-quarter, (27% [6/22]) of those who received an ESA had a Hgb value ≥ 12 g/dL, the maximum recommended threshold for use of these medications. Of the 18 residents that had blood pressure measurements, 18% (2/18) were hypertensive.

Conclusion—Suboptimal prescribing and monitoring of ESAs were common in the NHs we studied. Future studies are needed to determine if the development and use of computerized decision support systems can improve prescribing and monitoring of ESAs in the NH setting.

Keywords

Hematologic agents; hematinics; nursing homes; aged

INTRODUCTION

Anemia is defined by the World Health Organization as hemoglobin (Hgb) concentrations below 12 g/dL for women and 13 g/dL for men.[1] According to this case definition, approximately 50% of all nursing home (NH) residents have anemia.2 Diagnosing and treating anemia is particularly important, since it is an important predictor of morbidity and mortality, 3–5 and is associated with poor quality of life,6 falls,7 and impaired cognitive and functional status.8, [9] Recent evidence suggests that the majority of anemia amongst NH residents is associated with chronic kidney disease (CKD).[10, 11] Anemia secondary to CKD occurs primarily from a reduction in erythropoietin secretion by the kidneys.12

Anemia of CKD can be treated with the Food and Drug Administration (FDA) approved erythropoiesis stimulating agents (ESAs), epoetin alfa (Epogen and Procrit) and darbepoetin alfa (Aranesp).13, 14 Although these medications have generally been shown to be effective, there is increasing concern about their safety when prescribed inappropriately in certain high-risk populations (e.g., those with breast, non-small cell lung, head and neck, lymphoid, and cervical cancers).15–17 Moreover, recent evidence suggests that patients that are prescribed ESAs and have inadequate monitoring (e.g., hemoglobin value ≥ 12 g/dL, the maximum recommended threshold for use of these medications) have an increased risk of serious cardiovascular events and death.18, 19

One approach to detecting drug prescribing and monitoring problems is conducting drug-use evaluations.[20, 21] Drug-use evaluations have been used to describe problems with ESA prescribing and monitoring in ambulatory care, hemodialysis clinics, and inpatient settings.[22–24] However, little is known about the appropriateness of prescribing and monitoring of ESAs in the NH setting, where approximately 1.6 million Americans receive health care in more than 16,000 NHs annually.[25] The specific objectives of this study were to conduct a drug-use evaluation in order to determine the prevalence and appropriateness of prescribing and monitoring of ESAs in the NH setting.

METHODS

Study Design, Patients, and Setting

This cross-sectional study included all NH residents if they were prescribed at least one dose of an ESA and resided in one of the four community-based, independently owned, nonprofit NHs affiliated with the University of Pittsburgh Medical Center (UPMC) during the study period. One NH is in an urban setting, and the others are in suburban settings. The four NHs had a total of 532 beds, with an average bed size of 133 and range between 59–178. The study was approved by the UPMC Total Quality Council as a Quality Improvement study.

Drug-Use Evaluation Criteria

We conducted a drug-use evaluation in accordance with the guidelines set forth by the American Society for Health-System Pharmacists (ASHP).[20] ESAs included in this study were epoetin alfa and darbepoetin alfa. The complete prescribing and monitoring criteria utilized for the drug-use evaluation originated from FDA package inserts, supplemented with data from a recent survey to determine the minimal frequency of laboratory monitoring of steady state medications used in the NH setting (see Box).[13, 14, 26] We operationalized hypertension using the Joint National Committee (JNC) VII criteria (i.e., blood pressure ≥140/90 mmHg).[27] Specifically, we evaluated whether or not there was an appropriate FDA indication, if weight-based dosing was used, if iron supplements were co-administered, and if hemoglobin and blood pressure determinations were completed and were appropriate. We operationally defined appropriate prescribing and monitoring as meeting all FDA package insert recommendations.

Data Collection and Analysis

Consultant pharmacists with advanced training in geriatric pharmacy practice (SS and MA) conducted a retrospective chart review of all NH residents during a one-month study period from January to February, 2008. To complete the chart review, medical records, laboratory test results, diagnostic test results, and medication lists, were reviewed. For all eligible residents, the data that were collected included basic demographic information (age, gender, race, and weight), ESA indication (using International Classification of Diseases, 9th Revision of Codes ICD-9), ESA dosage (in mcg/kg or U/kg), weight (in kg), concurrent administration of any iron supplement, laboratory measurement of hemoglobin (Hgb), and blood pressure measurements. All chart review data was entered into a Microsoft Excel spreadsheet prior to analysis. We used descriptive statistics (i.e., percentages, means, and standard deviations) to summarize the data.

RESULTS

During the study period, a total of 4.5% (22/485) of the 485 NH residents received at least one dose of an ESA. Residents who received ESAs had a mean age of 80.4 (± 14.5) years. Most residents who received ESAs were female (64% [14/22]) and white (68% [15/22]), and had a mean weight of 72.0 (± 20.84) kg.

Overall, only 9% (2/22) of the residents met all of the drug-use evaluation criteria. Only 27% (6/22) of residents were prescribed an ESA for an FDA-approved indication and all had a diagnosis of anemia of CKD (Table). Other residents who had been prescribed an ESA had non–FDA-approved indications that included unspecified anemia (11/22), anemia of chronic disease (4/22), and erythropoietin-resistant anemia (1/22). Darbepoetin alfa was the most commonly prescribed ESA (64% [14/22]) followed by epoetin alfa (37% [8/22]). The mean weekly dose of darbepoetin alfa was 70.8 mcg (± 68.1 mcg) and the mean weekly dose of epoetin alfa was 22,625 (± 21,238) units. Almost one-quarter (23% [5/22]) of residents who were prescribed an ESA were not dosed according to weight-based guidelines, and all five of these residents had been prescribed a higher than recommended dose. The majority of those who received an ESA (64% [14/22]) had concurrent iron supplementation as recommended, and only one resident had iron levels within normal values.

All residents who received an ESA had at least one hemoglobin measurement during the study duration period. However, more than one-quarter, (27% [6/22]) of those who received an ESA had a Hgb value ≥ 12 g/dL. All but 4 of the residents who were received an ESA had their blood pressure measured during the study period. Of the 18 residents that had blood pressure measurements, 18% (2/18) were hypertensive.

DISCUSSION

Our application of drug-use evaluation criteria revealed that ESAs were suboptimally prescribed and monitored in the NHs studied. Conducting a drug-use evaluation is a necessary initial step to identify a potential problem that may require the development of a systems-based solution such as computerized decision support systems.[20] To the best of our knowledge, this represents the first study conducted to evaluate the prevalence and appropriateness of prescribing and monitoring of ESAs in the NH setting.

In our study, over two-thirds of residents were prescribed an ESA for an off-label indication. This degree of suboptimal prescribing is considerably higher than the frequency of off-label prescribing observed in ambulatory care and hospital-based studies.[24, 28, 29] For example, Patkar et al., conducted a retrospective study in the hospital setting, and concluded that approximately 50% of inpatient ESA prescriptions were for an off-label indication.[29] Clapp et al., conducted a study of a pharmacist-led intervention to improve ESA use at an ambulatory care clinic within the Veterans Administration.[22] Prior to initiating their intervention, they found that 53% of the patients had a FDA-approved indication for using ESAs.

Similar to other studies, our findings support that suboptimal laboratory monitoring of ESAs is common. Our results indicated that more then one-quarter of NH residents had a Hgb value $\geq$ 12 g/dL, the maximum FDA-recommended threshold for use of these medications. This is of particular concern, as there is a significant association between elevated hemoglobin values and increased risk of serious cardiovascular events and death in those receiving ESAs.[19] Armstrong et al., also reported suboptimal monitoring of various hematologic tests, including hematocrit, ferritin and transferrin saturation measurements not being done in a timely fashion in those receiving ESAs in a dialysis clinic.[23] The authors also noted that dose reductions were not made in response to elevated hematocrits.

Our study has several limitations. First, we performed a cross-sectional study that was limited to a single month. It is possible that seasonal or other variations may affect the validity of the results. Second, we did not include in our evaluation some of the monitoring parameters that are recommended by the package inserts prior to the initiation of ESA therapy, including serum ferritin and serum transferrin. As a result, it is possible that we have underestimated the frequency of suboptimal monitoring. However, there were no new prescriptions for an ESA during the study period, as all were being used chronically. Third, we selected four NHs with largely similar institutional characteristics, located in a single geographic region, and affiliated with an academic medical center. This may limit the generalizability of our results to other NHs.

Further research is needed in several aspects of ESA prescribing and monitoring. First, additional research is needed to validate our findings in NHs with differing facility characteristics and over a longer period of time. Second, future research should characterize the association between differing provider and facility characteristics and suboptimal prescribing and monitoring of ESAs. Third, research is needed to study the impact of the development and use of computerized decision support systems on resident and provider outcomes associated with ESA prescribing and monitoring.

CONCLUSION

Suboptimal prescribing and monitoring of ESAs were common in the NHs we studied. Future studies are needed to determine if the development and use of computerized decision support systems can improve prescribing and monitoring of ESAs in the NH setting.

Box

Drug-use evaluation criteria for erythropoiesis stimulating agents [13, 14, 26, 27]

Prescribing parameters, FDA approved indications for use

- Anemia of chronic kidney disease (CKD)
- Anemia associated with zidovudine-treated HIV patients
- Anemia associated with cancer patients with non-myeloid malignancies and concomitant chemotherapy-induced anemia
- Reduction of allogenic blood transfusion in surgery patients undergoing elective, non-cardiac, non-vascular surgery

Additional prescribing parameters

- Weight-based dosing
  - Darbepoetin alfa: 0.45 mcg/kg IV/SC weekly
  - Epoetin alfa: 50–100 Units/kg three times a week
- Co-prescribing of iron supplement (independent of formulation, dose or frequency)

Monitoring parameters

- Hemoglobin determinations (hemoglobin value ≥ 12 g/dL, the maximum recommended threshold for use of these medications)
- Blood Pressure determinations (hypertension defined as a blood pressure ≥ 140/90mmHg)

Acknowledgments

This study was supported in part by NIH grants 5KL2RR024154 (NIH Roadmap Multidisciplinary Clinical Research Career Development Award Grant), 5T32AG021885, P30AG024827, R01AG027017, R01AG0135, a Pittsburgh VA GRECC Pilot grant, and a VA HSR&D merit proposal (IIR-06-062). Additionally, the authors acknowledge no conflicts of interest.

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Table

Drug-use evaluation results

Criteria	Number of nursing home residents
FDA-approved indications:	
• Anemia of chronic kidney disease (CKD)	6
• Anemia associated with zidovudine-treated HIV patients	0
• Anemia associated with cancer patients with non-myeloid malignancies and concomitant chemotherapy-induced anemia	0
• Reduction of allogenic blood transfusion in surgery patients undergoing elective, non-cardiac, non-vascular surgery	0
Off-label indications:	
• Unspecified anemia	11
• Anemia of chronic disease	4
• Erythropoietin-resistant anemia	1
On any iron supplementation	14
Dosing appropriate to weight	17
Hemoglobin > 12 g/dL	6
Hypertension (Systolic > 140, Diastolic > 90)	5
Blood Pressure not measured	4