Pharmacist-driven epoetin alfa-epbx dosing for hospitalized patients

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Purpose: To determine the effectiveness of pharmacy consultation in managing epoetin alfa-epbx dosing for inpatients on hemodialysis.

Methods: This multisite, retrospective cohort study evaluated the implementation of an initial dose consultation for epoetin alfa-epbx by pharmacists. A pre-post cohort study evaluated patients from August 2020 through January 2021 and August 2021 through January 2022, respectively. Hospitalized patients were included if they were at least 18 years of age, received hemodialysis, and were administered an erythropoiesis-stimulating agent (ESA) for anemia due to chronic kidney disease. Patients were excluded for religious objections to receiving blood products or if patients were discharged or died before their first hemodialysis session. The primary outcome was the average epoetin alfa-epbx acquisition cost per patient. Secondary endpoints were the epoetin alfa-epbx overall pharmacy purchasing cost, the average dose, and the number of administered doses. A subgroup analysis was performed for patients in the post group with an outpatient ESA before admission to determine the epoetin alfa-epbx days saved.

Results: A total of 264 patients were included in the pre group, and 272 patients were included in the post group. The average acquisition cost was significantly lower in the post group ($1,681.77 vs $1,041.35, $P < 0.0001$). The overall pharmacy purchasing cost was also lower in the post group ($148,970.89 vs $127,873.25). The post group had a significantly lower average dose (13,694 vs 10,112 units, $P = 0.0004$), while the number of administered doses did not differ significantly between the groups (2.09 vs 1.79 doses, $P = 0.0668$). The subgroup analysis included 83 patients, which yielded 53 epoetin alfa-epbx days saved.

Conclusion: Pharmacist-driven ESA dosing was associated with significant decreases in ESA average acquisition cost and average total dose per patient.

Keywords: epoetin alfa, erythropoiesis, nephrology, pharmacists, pharmacy, renal dialysis

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Epoetin alfa-epbx is an erythropoiesis-stimulating agent (ESA) used primarily to treat anemia due to chronic kidney disease (CKD) in patients receiving or not receiving hemodialysis.[1] Epoetin alfa-epbx is also indicated for anemia caused by zidovudine in patients with HIV infection, anemia due to myelosuppressive chemotherapy, and for reduction of allogenic red blood cell (RBC) transfusions for elective, noncardiac, nonvascular surgery.[1] As epoetin alfa-epbx is a high-cost, high-utilization medication, proper dosing can result in significant cost savings and prevent inappropriate dosing. One prior study assessed ESA utilization outside the intensive care unit using guideline-based criteria during a 2-week period. The authors found that 14% of patients were not appropriately monitored with iron studies and 24% of patients had untreated iron deficiency, resulting in approximately $14,000 and $24,000

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worth of excessive ESA doses, respectively.[2] Other prior studies have focused on outpatient anemia clinics with pharmacist-driven protocols and have found that pharmacists are responsible for improving outcomes, shortening the time to the therapeutic range, reducing adverse events, and reducing costs.[3-6]

Patients on outpatient hemodialysis may require an ESA while in the inpatient setting for continuity of care. In the outpatient setting, patients are typically on methoxy polyethylene glycol-epoetin beta given its monthly or biweekly dosing frequency.[7] Patients may be started on an ESA in the inpatient setting without consideration of their outpatient dosing regimen or the last date of administration. As a result, inappropriate or excessive dosing may occur. By not continuing an ESA in the inpatient setting, a patient's hemoglobin may not be at an adequate level, leading to potentially more blood transfusions.

Our health system implemented a pharmacy consultation that enabled pharmacists to manage initial ESA dosing. The goal for implementing this consultation was to have a large clinical and financial impact while minimally impacting workflow by focusing on ESA initial dosing and deferring to the physician for anemia workups for iron and vitamin B_{12}. Overall, this research project aimed to evaluate the impact of pharmacy ESA consultation on inappropriate dosing and identify cost savings associated with consultation.

KEY POINTS

- Erythropoiesis-stimulating agents (ESAs) are a high-cost, high-utilization medication that can significantly impact a health system's financial expenditure if left unchecked.
- Pharmacists are in a prime position to optimize ESA dosing upon hospital admission and ensure appropriate transitions of care with regard to timing of ESA doses to minimize inappropriate or excessive ESA dosing.
- A pharmacist-driven ESA consult was associated with a significant decrease in average acquisition cost and average dose per patient.

Objective

The purpose of this study was to assess the implementation of pharmacist-driven ESA dosing for hospitalized patients on hemodialysis.

Implementation process

Study design. This multisite, retrospective cohort study was conducted within a health system comprising a level II trauma center and 3 community hospitals with a combined total of 868 beds. The pre group included patients from August 2020 through January 2021, and the post group included patients from August 2021 through January 2022. The same 6-month period was selected for both groups to assist in mimicking any yearly trends among patients. The study was approved by the health system's ethics committee.

Setting. A pharmacist-led epoetin alfa-epbx initial dose consultation was implemented on July 28, 2021. Pharmacist education was provided as an in-service session that highlighted key points and provided telephone numbers for local dialysis centers. Nephrologists consulted pharmacists through a hemodialysis order set or order browse. The consultation was an opt-out feature and was the default on the order set. The pharmacist then reviewed the patient's profile to determine whether the patient was a new hemodialysis start or if he or she was on outpatient hemodialysis. If the patient had an outpatient hemodialysis center, the pharmacist contacted the center to determine whether the patient was on an ESA in the outpatient setting. If so, the pharmacist collected the following information: name of the medication, dose, frequency, and next date for which administration was scheduled. The pharmacist utilized a conversion table (Table 1) to assist in converting outpatient doses, which consisted mostly of methoxy polyethylene glycol-epoetin beta, to epoetin alfa-epbx. The conversion table was developed from information obtained from the package inserts of epoetin alfa-epbx and methoxy polyethylene glycol-epoetin beta. Epoetin alfa-epbx was chosen because of its formulary status, which is due to financial preference and a dosing frequency that mimics outpatient dialysis schedules. Pharmacists used clinical judgement for outpatient doses that were outside of the ranges in the conversion table and considered patient-specific factors, including hemoglobin, hematocrit, and serum ferritin levels; transferrin saturation; last ESA dose; and prior ESA dose titrations. If a patient was not on an ESA in the outpatient setting, the pharmacist entered a rounded dose of 50 units/kg intravenously 3 times weekly. The patient's hemoglobin concentration was assessed the day the dose was due, and the epoetin alfa-epbx order had a hold parameter for a hemoglobin concentration greater than 11 g/dL. Interventions were recorded in the electronic health record (EHR) that is shared across the health system, with

Table 1. Erythropoiesis-Stimulating Agent Conversion Chart

Epoetin alfa-epbx	Methoxy polyethylene glycol-epoetin beta
<8,000 units/week	120 µg once monthly or 60 µg every 2 weeks
8,000 to 16,000 units/week	200 µg once monthly or 100 µg every 2 weeks
>16,000 units/week	360 µg once monthly or 180 µg every 2 weeks

specific details recorded in the order entry item.

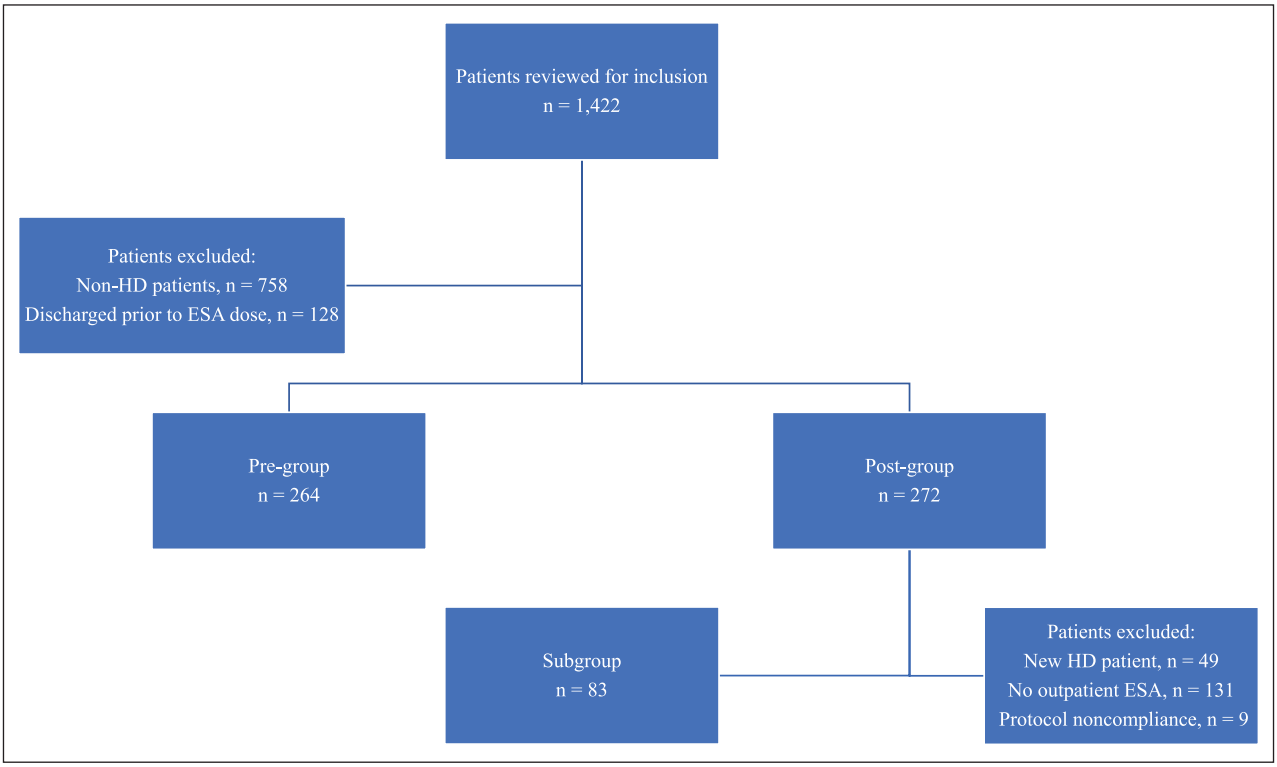
Patient enrollment. Patients were included in the study if they were hospitalized, at least 18 years of age, received hemodialysis, and received an ESA for anemia due to CKD (Figure 1). Patients were excluded from the study if they had religious objections to receiving blood or blood products or if the patients were discharged or died before their first hemodialysis session, before an ESA was administered. Patients from the post group were enrolled in a subgroup if they received an ESA from an outpatient hemodialysis center.

Data collection and analysis. Patient data were collected and analyzed using the Sunrise Clinical Manager (Altera Digital Health) and Allscripts Clinical Performance Management (Allscripts Healthcare Solutions, Chicago, IL). Statistical analysis was conducted using JMP Pro 15 (SAS Institute, Cary, NC), which utilized a Student's t test or a χ^2 test as appropriate. A P value of <0.05 was deemed statistically significant for both tests. The primary outcome was the average acquisition cost of epoetin alfa-epbx per patient. Secondary outcomes included the average monthly purchasing cost during the study period, the overall purchasing cost of epoetin alfa-epbx during the study period, the average dose of epoetin alfa-epbx, the average number of administered doses per patient, the percentage of patients experiencing stroke or thrombosis, and the percentage of patients receiving blood transfusion(s) during admission. Subgroup analysis examined the number of epoetin alfa-epbx days saved through the proper timing of ESA doses.

Results

A total of 1,422 patients were reviewed for inclusion, with the pre group consisting of 264 patients and the post group consisting of 272 patients. A total of 886 patients were excluded from the study (Figure 1). Baseline characteristics did not differ significantly between the 2 groups (Table 2). For the primary outcome, the post group had a statistically significant reduction in the average acquisition cost per patient ($1,681.77 vs $1,041.35, $P < 0.0001$) (Table 3). During the study period, the difference in average monthly purchasing cost between the groups was not statistically significant ($24,828.48 vs $21,312.21, $P = 0.5594$) and the difference in overall purchasing cost between the pre and post groups was $21,097.64 ($148,970.89 vs $127,873.25). Additionally, the average dose was significantly lower in the post group (13,694 vs 10,112 units, $P = 0.0004$). The post group had a decrease in the average number of administered doses per patient, but this decrease was not found to be statistically significant (2.09 vs 1.79 doses, $P = 0.0668$). Differences between the 2 groups in the incidence of stroke, thrombosis, and RBC transfusion during admission were not statistically significant. A total of 189 patients (69.5%) had not been on an ESA in the outpatient setting. In the subgroup analysis, 83 patients (30.5%) had received ESA therapy in the outpatient

Figure 1. Study diagram. ESA indicates erythropoiesis-stimulating agent; HD, hemodialysis.



setting before hospitalization, with a combined total of 53 epoetin alfa-epbx days saved.

Discussion

This study provides support for previous findings of improved outcomes and reduced costs when pharmacists are involved with ESA dosing. Prior pharmacist-led ESA initiatives focused on outpatient anemia clinics or inpatient anemia protocols.[2,4,5] They did not significantly focus on inpatient ESA dosing and instead examined laboratory monitoring for iron status and vitamin B_{12} levels. To our knowledge, this study is the first that specifically addresses a pharmacist's impact on initial dosing of an ESA. The pharmacist-led consult was associated with a significant decrease in the average acquisition cost and average dose per patient. While the differences in average monthly purchasing cost and average number of administered doses between the 2 groups were not statistically significant, a decrease was observed for both parameters in the post group. The focus on the subgroup was to identify potential cost savings in patients who are on an ESA in the outpatient setting and prevent excessive ESA dosing. While most patients did not meet the criteria for inclusion in the subgroup analysis, it may still be clinically significant for pharmacists to contact outpatient hemodialysis centers and appropriately time epoetin alfa-epbx doses. For instance, significant savings can be seen if a patient is admitted shortly after they received an outpatient ESA. This would result in their next dose being scheduled 2 to 4 weeks in the future, leading to multiple epoetin alfa-epbx days saved.

One strength of this study was that it was conducted across multiple hospitals, which increased the possible pool of patients and helps to increase generalizability. Another strength was the education and standardized workflow provided to pharmacists. The workflow helped reduce variability among pharmacists and ensured that pharmacists knew how to document any interventions, both of which contributed to ease of data collection and increased reliability and validity among pharmacists.

Limitations and challenges. Limitations to this study included its retrospective nature, which could have resulted in bias, and unmeasured variables, which could have influenced the results. Another possible limitation was the multiple changes to the ESA dialysis order sets. Before implementation of the consult, the ESA order set had options for epoetin alfa-epbx 10,000 units 3 times weekly and 40,000 units weekly; following implementation, the order set was streamlined, removing the options to easily order these large doses of epoetin alfa-epbx. Therefore, the consultation by itself may have yielded a less significant cost savings, while the larger cost savings may have resulted from the combination of order set changes and pharmacy consultation. Additionally, time spent performing the consultation was not measured. When reviewing the consults, it was estimated that each consultation took approximately 5 minutes depending on the timeliness of the conversation with the dialysis center. While this is not a significant amount of time, this task could be delegated to pharmacy

Table 2. Patient Characteristics

Characteristic	Pre group (n = 264)	Post group (n = 272)	*P* value
Age, mean (SD), years	63.61 (14.47)	61.54 (15.43)	0.1231
Sex (female), %	43.97	41.18	0.5876
Weight, mean (SD), kg	81.19 (25.42)	83.49 (27.58)	0.3306
Height, mean (SD), cm	167.90 (11.50)	169.36 (11.68)	0.1588
BMI, mean (SD), kg/m^2	29.26 (15.23)	29.08 (8.96)	0.8753

Abbreviation: BMI, body mass index.

Table 3. Summary of Results

Outcome	Pre group (n = 264)	Post group (n = 272)	*P* value
Acquisition cost per patient, mean (SD)	$1,681.77 ($1,425.45)	$1,041.35 ($1,172.16)	<0.0001
Monthly purchasing cost during the study period, mean (SD)	$24,828.48 ($5,979.71)	$21,312.21 ($12,732.88)	0.5594
Overall purchasing cost during the study period	$148,970.89	$127,873.25	NA
Dose, mean (SD), units	13,694 (12,112)	10,112 (11,901)	0.0004
Administered doses per patient, mean (SD)	2.09 (1.81)	1.79 (2.01)	0.0668
Stroke during admission, No. (%)	6 (2.26)	5 (1.84)	0.7323
Thrombosis during admission, No. (%)	29 (10.9)	30 (11.03)	0.9624
Red blood cell transfusion during admission, No. (%)	93 (34.96)	111 (40.81)	0.1623

Abbreviation: NA, not applicable.

technicians, interns, or residents to alleviate the burden on pharmacists.

Another limitation was that pharmacists did not assess how long a patient was on an ESA in the outpatient setting before admission when performing the consult. The ESA was either converted or entered as the standard dose. The patient's hemoglobin concentration was then assessed on the day the dose was due, and the dose was held if the patient's hemoglobin concentration was greater than 11 g/dL. When analyzing RBC transfusions, a procedure code was collected and the number of units transfused per patient was not collected. Additionally, pharmacists did not assess other dialysis-related medications, but it would be important to determine a patient's iron status to ensure optimal clinical outcomes from receiving an ESA. This assessment was not performed as it could have increased the time to complete the consultation or resulted in additional workflow interruptions.

Future directions. On the basis of the results of this study, pharmacists will continue to manage initial ESA dosing for hemodialysis patients. Moving forward, the consult may be expanded to include other ESA indications, such as for nonhemodialysis or oncology patients, or to include inpatient anemia screening, monitoring, and outpatient transition for hemodialysis patients. Other hospitals and health systems may consider evaluating their ESA utilization to identify whether developing a similar pharmacist-led consult may lead to increased appropriateness of ESA dosing, a reduction in ESA cost, and improved transitions-of-care opportunities.

Conclusion

Implementation of a pharmacist-driven initial ESA dosing consultation may provide pharmacists the ability to reduce inappropriate or excessive ESA dosing, resulting in reduced costs and improved transitions of care for hemodialysis patients on hospital admission.

Disclosures

The authors have declared no potential conflicts of interest.

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