EPO Adjustments in Patients With Elevated Hemoglobin Levels: Provider Practice Patterns Compared With Recommended Practice Guidelines

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Background: This study investigates provider practices regarding recombinant human erythropoietin (rHuEPO) dose when patient hemoglobin levels exceeded National Kidney Foundation–Dialysis Outcomes Quality Initiative target levels and reached 13 g/dL or greater (≥130 g/L).

Methods: The study population (N = 167,796) was hemodialysis patients prevalent on January 1, 2003, who were on renal replacement therapy at least 90 days with Medicare as primary payer and rHuEPO claims in 2 or more consecutive months. Patient characteristics were obtained from the Centers for Medicare & Medicaid Services (CMS) Medical Evidence Report, and comorbid conditions were determined from Medicare claims. Providers and rHuEPO claims were linked by using CMS-assigned provider numbers and the CMS Annual End-Stage Renal Disease Facility Survey. Between-provider differences in patient characteristics were examined by using chi-square test, and provider effect on appropriate response, by using logistic regression.

Results: DaVita's percentage of monthly claims for patients with hemoglobin levels of 13 g/dL or greater (≥130 g/L; 16.7%) and mean monthly rHuEPO dose (54,299 units) were highest. Dialysis Clinic Inc's percentage of such claims (2.0%) and mean monthly dose (38,687 units) were lowest. Dialysis Clinic Inc, Fresenius, and Renal Care Group had the highest percentage of recommended dose adjustments (mean, 70% of units); hospital-based units had the lowest (59%). By adjusted odds ratio, adjustments were 20% more likely for Dialysis Clinic Inc, Fresenius, and Renal Care Group compared with DaVita, National Nephrology Associates, hospital-based units, and independents (17% to 28% less likely).

Conclusion: rHuEPO dose reduction practices are dependent on specific dialysis providers and whether units are hospital based or independent.

Am J Kidney Dis 49:135-142. © *2006 by the National Kidney Foundation, Inc.*

INDEX WORDS: Hematocrit; hemodialysis (HD); hemoglobin; recombinant human erythropoietin.

The introduction of recombinant human erythropoietin (rHuEPO) into clinical practice for the treatment of anemia related to end-stage renal disease (ESRD) led to substantial improvements in hemoglobin levels.[1,2] The dramatic increase in mean hemoglobin levels from the early 1990s to 2003 is paralleled by similar increases in rHuEPO doses and iron management.[3]

Target hemoglobin levels became an important aspect of care in autumn 1997, with the introduction of clinical practice guidelines by the National Kidney Foundation under its Dialysis Outcomes Quality Initiative. These guidelines, which were developed from the US Food and Drug Administration (FDA) labeling indication for epoetin, intervention trials, and expert opinion, suggested a target hemoglobin level of 11.0 to 12.0 g/dL (110 to 120 g/L) with rHuEPO treatment.[4] Providers' ability to maintain hemoglobin levels within the target range has been a matter of concern, given natural variability and other clinical factors that interfere with rHuEPO effectiveness.[5,6] Centers for Medicare & Medicaid Services (CMS) payment policies requiring medical justification for rHuEPO treatment when hematocrit levels exceeded 37.5%, with possible auditing for repayment, also may have contributed to variability. Cross-sectional data gathered

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Received May 10, 2006; accepted in revised form September 22, 2006.

Originally published online as doi:10.1053/j.ajkd.2006.09.020 on December 1, 2006.

Support: This study was supported by an unrestricted research grant from Amgen Inc, Thousand Oaks, CA. Potential conflicts of interest: A.J.C. and D.T.G. have received consulting fees from Amgen. J.P.E., none.

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0272-6386/06/4901-0016$32.00/0

doi:10.1053/j.ajkd.2006.09.020

monthly indicate that approximately 30% of patients have hemoglobin levels less than 11 g/dL (<110 g/L), 36% have levels between 11 and 12 g/dL (110 to 120 g/L), and the remaining third have hemoglobin levels greater than 12 g/dL (>120 g/L). Although this overall distribution appears to be consistent month to month, few patients remain within a particular group, such that by year end, only 5% are still in their original groups.[5,6]

The increasing percentage of patients with hemoglobin levels exceeding the current National Kidney Foundation–Kidney Disease Outcomes Quality Initiative (KDOQI) target level of 12 g/dL (120 g/L) has been accompanied by a decreased percentage of patients with hemoglobin levels less than 11 g/dL (<110 g/L).[7] These developments appear to be the result of many factors, including concurrent illnesses, fluid overload leading to hemodilution, and rHuEPO hyporesponsiveness. However, as reported by the US Renal Data System (see *Annual Data Report* chapters on providers and economic costs),[3] there is considerable variation among dialysis providers in the distribution of patient hemoglobin levels. The increasing percentage of patients with hematocrits greater than 39% has caused concern because findings in at least 1 clinical trial suggested that high hematocrits (close to 42%) may constitute a risk for vascular access thrombosis and potentially increased mortality.[8] The recommended hemoglobin level range was defined on the basis of clinical trials suggesting safety at lower levels, but providers may not always decrease doses accordingly. Lack of attention to these targets, particularly at the upper end of the range, may lead to overuse of rHuEPO, driving hemoglobin to higher levels and overshooting the target range.

Recently, a new policy for rHuEPO use was implemented by the CMS.[9] It requires reduction in payment for rHuEPO doses for patients with hematocrits of 39% or greater. It is unclear how frequently providers adjust doses and whether there are differences across large groups. In this study, we investigate provider practice patterns related to rHuEPO dose and its adjustment when patient hemoglobin levels were at least 13 g/dL (130 g/L), a level consistent with CMS monitoring policy for use by fiscal intermediaries.

METHODS

The study population (N = 167,796) consisted of hemodialysis patients prevalent on January 1, 2003, who had been receiving renal replacement therapy for at least 90 days as of January 1, 2003; had Medicare as primary payer; and had rHuEPO claims in at least 2 consecutive months. Patient characteristics (age, sex, race, primary cause of renal failure, and dialysis vintage) were obtained from the CMS Medical Evidence Report (CMS-2728). Comorbid conditions were determined from Medicare Part A institutional and Part B physician/supplier claims, using *International Classification of Diseases, Ninth Revision, Clinical Modification,* codes according to a previously described method.[10] Conditions characterized included atherosclerotic heart disease, congestive heart failure, cardiac arrhythmia, other cardiac disease, cerebrovascular accident/transient ischemic attack, peripheral vascular disease, chronic obstructive pulmonary disease, cancer (including melanoma, but not skin cancer), liver disease, and gastrointestinal bleeding.

All rHuEPO claims for the study population for 2003 were analyzed to characterize anemia management, with specific attention to claims with a reported hemoglobin level of at least 13 g/dL (130 g/L). For each such claim, the rHuEPO dose was compared with the dose reported on the rHuEPO claim for the next month. To reduce the potential for incomplete dosing information, only claims for months in which the patient was not hospitalized were considered. KDOQI guidelines and the FDA-approved manufacturer's recommendations for anemia management call for a dose reduction of 25% for patients with a hemoglobin level of at least 12 g/dL (120 g/L). Recognizing the difficulty maintaining levels at the upper end of the recommended range (12 g/dL [120 g/L]) without exceeding it and based on the new CMS payment policy, we used a cutoff point for dose reduction 1 g/dL greater than the recommended level. Because claims data generally yield rHuEPO dosing information for 1 claim per month, we could detect dosage changes only from one month to the next, but the dose could have changed at any time during the month. To accommodate this imprecision, we classified a month-to-month dose reduction of one half the guideline (ie, 12.5% reduction) as an appropriate response to a hemoglobin level of at least 13 g/dL (130 g/L).

Using the CMS-assigned provider number included on the rHuEPO claim and the CMS Annual ESRD Facility Survey, rHuEPO claims were linked to individual dialysis providers, which were analyzed by chain (DaVita, Dialysis Clinic Inc, Fresenius, Gambro, National Nephrology Associates, and Renal Care Group). Providers not part of a chain were classified as hospital based or independent, defined from the CMS facility survey. If CMS identified a unit as hospital based, we classified it as hospital based. If CMS identified a unit as freestanding and it was not a part of 1 of the major chains named, we classified it as independent. Provider numbers that could not be linked to ESRD Facility Survey data were classified as "unknown affiliation." Providers with fewer than 10 qualifying rHuEPO claims were excluded from analysis.

For each provider, a measure of anemia management was calculated as the number of appropriate responses (rHuEPO