To study the association between ESAhr and mortality in HD patients

To determine a contemporary definition of ESAhr that is relevant to current

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Adjusted models contained fixed-effects terms for covariates that differed significantly between

patient met the operative definition of ESAhr (definition 4) at any point during Q1 2012. Patients

were considered. Exposure status was assigned as ESAhr or non-ESAhr based on whether the

time.

• In cases where adjusted models did not converge, changes in covariate adjustments were

necessary on a model-by-model basis, based on the variables presumed to have the least

6 months to ensure stable ESA use.

• Energy was highly prevalent among patients with end-stage renal disease (ESRD) and is associated with poor outcomes and mortality.6 Renal anemia in patients with ESRD receiving hemodialysis (HD) is typically treated with both erythropoiesis-stimulating agents (ESAs) and intravenous (IV) iron.5,6

• Many HD patients with renal anemia do not respond optimally to ESA treatment (ie, are ESA-hyporesponsive [ESAhr]). ESAhr patients are unable to achieve their targeted hemoglobin (Hb) concentration or require chronic high ESA doses to achieve their targets.4

• Prior studies have examined the association between ESAhr and outcomes among HD patients.7–9

• However, none have been conducted following 2011 changes to the US ESA labels and reimbursement policy, using recent data and a definition of ESAhr that is relevant to contemporary practice.

Introduction

Objects

• To determine a contemporary definition of ESAhr that is relevant to current ESA-dosing practices

• To study the association between ESAhr and mortality in HD patients

Methods

• Eligible patients were 18 years of age or older, non-neovascular, receiving in-center HD at a dialysis organization (DO), and had a dialysis vintage ≥ 6 months to ensure stable ESA use.

• Point prevalence for various definitions of ESAhr was determined at the beginning of each consecutive calendar quarter (Q) during the study period (01 Jan 2012-31 Dec 2013) by dividing the number of patients meeting the definition criteria by the total number of patients eligible at the time.

• For associative analysis, the point prevalent cohort eligible of ESAhr patients at the start of Q2 2012 were considered. Exposure status was assigned as ESAhr or non-ESAhr based on whether the patient met the operative definition of ESAhr (definition 4) at any point during Q2 2012. Patients were followed until the earliest of death, loss to follow-up (transfer of care, death, transplantation, enrollee discontinued in the DO), or end of study (31 Dec 2013).

• ESA utilization was calculated monthly as the mean administered per dialysis session. Hemoglobin was determined as the mean of all measurements during the month. Onsets and missed dialysis treatments were assessed quarterly and expressed as the rate (number of events during the quarter divided by cumulative time at risk).

• Associations of ESAhr status with ESA utilization and hemoglobin concentration were estimated using general estimating equation linear models with an identity link and Gaussian distribution. Models contained fixed-effects terms for exposure status (ESAhr or non-ESAhr) and time (quarterly), and a quadratic time term to account for differences over time in the association between exposure groups.

• Associations of ESAhr status with mortality and missed dialysis treatments were estimated using general estimating equation models using a log-log link and Poisson (hazard ratio [HR]) or negative binomial (adjusted incidence rate ratios) distribution.

• Adjustments contained fixed-effects terms for covariates that differed significantly between exposure groups at baseline (P < 0.10).

• In cases where adjusted models did not converge, changes in covariate adjustments were necessary on a model-by-model basis, based on the variables presumed to have the least influence on the final estimates.

Results

• The point prevalence of candidate definitions of ESAhr was assessed (Table 1). Definition 4 of ≥ 1700 U/treatment and consecutive Hb measurements (separated by at least 14 days) < 10 g/dL made the expected prevalence rate of approximately 10%5,6 and was used to define ESAhr in all subsequent analyses.

• Compared to non-ESAhr patients, ESAhr patients were younger, more likely to be African American, more frequently used central venous catheters, less frequently used arteriovenous fistulae, and were more frequently treated with antibiotics (Table 2).2

• ESAhr patients had significantly greater ESA and IV iron utilization (Figure 1A and 1B) and lower Hb concentrations (Figure 1C) compared to non-ESAhr patients at all time points during follow-up.

• ESAhr was associated with a greater adjusted risk of mortality versus non-ESAhr in Q2 through Q8 of follow-up (Figure 2). Adjusted incidence rate ratios (IRR; 95% confidence interval [CI]) ranged from 3.24 (1.53, 2.68) in Q2 of follow-up to 1.48 (1.18, 1.84) in Q8.

• ESAhr was associated with a greater rate of missed dialysis treatments versus non-ESAhr. Adjusted incidence rate differences (IRD; 95% CI) ranged from 2.46 (2.32, 2.52) in Q1 of follow up to 1.47 (1.36, 1.68) in Q8.

Conclusions

• We identified a definition of ESAhr that is relevant to contemporary clinical practice and expected disease prevalence.

• Using this definition we show that ESAhr is potent and persistently associated with:

– Increased ESA and IV iron use

– Lower Hb concentrations

– Elevated rates of mortality and missed dialysis treatments

References


Table 1. Apparent Prevalence of ESAhr by Candidate ESAhr Definitions

Table 2. Characteristics of ESAhr and Non-ESAhr Patients

Figure 1. ESA Utilization, IV Iron Utilization, and Hemoglobin Levels among ESAhr and Non-ESAhr Patients

Figure 2. Adjusted Associations between ESAhr, Mortality, and Missed Dialysis Treatments

Acknowledgments

• This study was supported by National Institutes of Health (grants K08DK085484, P01DK074554, P01DK074554-S1, R01DK093669, K08HL115920, R01DK109532, and R01HL131157 to J.L.), the Agency for Healthcare Research and Quality (grant 1U18HS023356 to J.L.), the L. Thomas and Kiko D. Leffler Foundation, and the DaVita Clinical Research Unit. J.L. had full access to all data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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