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Original Research Article

Factors associated with the receipt of antimicrobials among chronic hemodialysis patients

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Background: Antimicrobial use is common among patients receiving chronic hemodialysis (CHD) and may represent an important antimicrobial stewardship opportunity. The objective of this study is to characterize CHD patients at increased risk of receiving antimicrobials, including not indicated antimicrobials.
Methods: We conducted a prospective cohort study over a 12-month period among patients receiving CHD in 2 outpatient dialysis units. Each parenteral antimicrobial dose administered was characterized as indicated or not indicated based on national guidelines. Patient factors associated with receipt of antimicrobials and receipt of ≥1 inappropriate antimicrobial dose were analyzed.
Results: A total of 89 of 278 CHD patients (32%) received ≥1 antimicrobial doses and 52 (58%) received ≥1 inappropriately indicated dose. Patients with tunneled catheter access, a history of colonization or infection with a multidrug-resistant organism, and receiving CHD sessions during daytime shifts were more likely to receive antimicrobials (odds ratio [OR], 5.16; 95% confidence interval [CI], 2.72-9.80; OR, 5.43; 95% CI, 1.84-16.06; OR, 4.59; 95% CI, 1.20-17.52, respectively). Patients with tunneled catheter access, receiving CHD at dialysis unit B, and with a longer duration of CHD prior to enrollment were at higher risk of receiving an inappropriately indicated antimicrobial dose (incidence rate ratio, 2.23; 95% CI, 1.16-4.29; incidence rate ratio, 2.67; 95% CI, 1.34-5.35; incidence rate ratio, 1.11; 95% CI, 1.01-1.23, respectively).
Conclusions: This study of all types of antimicrobials administered in 2 outpatient dialysis units identified several important factors to consider when developing antimicrobial stewardship programs in this health care setting.

The outpatient hemodialysis unit is a high-risk setting for the acquisition of multidrug resistant organisms (MDRO).[1] A contributing factor is the substantial exposure to antimicrobials among patients requiring chronic hemodialysis (CHD).[2] At least 40% of patients on CHD receive ≥1 antimicrobial course each year, a frequency that exceeds the use of antimicrobials in nursing home populations, another patient population with high rates of MDRO.[3-5]

Studies focusing on antimicrobial use in the CHD population, including reasons for inappropriate administration, are limited.[6-8] We have previously published a prospective 12-month cohort study in 2 outpatient dialysis units characterizing antimicrobial use and reasons for inappropriate prescribing. In that study, over one-third of CHD patients received at least 1 antimicrobial course in the 12-month study period, and among all antimicrobials prescribed, one-third were classified as inappropriately indicated, based on national guidelines.[6,9-19] Vancomycin and third- and fourth-generation cephalosporins were the most common antimicrobials prescribed inappropriately. The 3 main reasons for inappropriate prescribing were (1) criteria for infection were not met based on

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national guidelines, (2) failure to choose a more narrow-spectrum antimicrobial, and (3) criteria for surgical prophylaxis were not met.[6]

To this evidence, which describes how antimicrobials are inappropriately prescribed, we present here additional data describing the characteristics of patients at higher risk of receiving antimicrobials, including those who received antimicrobials inappropriately, based on national guidelines. This information is integral to developing effective stewardship efforts with the goal of improving prescribing practices.

MATERIALS AND METHODS

Dialysis units

The study was conducted in 2 outpatient CHD units in Boston, Massachusetts. Each unit has an approximate point census of 100 patients and is affiliated with a community-based academic medical center. The study population has been previously described, including clinical characteristics of patients, antimicrobial use rates, and appropriateness of indication for antimicrobial receipt.[6] Study data were collected by a study investigator, and unit clinicians were blinded to study methodology. The conduct of this study was approved by the institutional review board at the investigator and participating medical center institutions.

Study population and data collection

Patients were included in the study if they were registered patients of the CHD unit and received at least 1 hemodialysis session for end-stage renal disease during the study period (August 2010-July 2011). Patients on peritoneal dialysis who received exclusively a backup session of dialysis while remaining on peritoneal dialysis and nonresidents receiving CHD while traveling were excluded. Demographic data were collected for each study patient at the time of enrollment, including age, sex, pertinent medical conditions and comorbidities, and CHD-related factors. The Charlson Comorbidity Index score, which has been validated in the CHD population, was used as a composite score of comorbidities.[20,21] MDROs included methicillin-resistant *Staphylococcus aureus*, vancomycin-resistant enterococci, and multidrug-resistant gram-negative bacteria. For each antimicrobial dose, comprehensive data supporting the indication for use were collected from available documentation in the unit and affiliated medical center electronic medical records.

Antimicrobial characterization

Only parenteral antimicrobial doses administered in the hemodialysis unit were evaluated. Each administered dose was categorized as having an appropriate or inappropriate indication; any dose for which there was inadequate or unavailable documentation in support of appropriate criteria was classified as unknown appropriateness. Criteria for the appropriateness of indication were defined a priori using published guidelines for each site of suspected infection.[6,9-19,22] The appropriateness of each dose was characterized based on the clinical data available to the prescribing clinician at the time the dose was administered. Doses characterized as inappropriate included antimicrobials prescribed empirically without guideline-based minimum criteria to define infection being met; antimicrobials prescribed for treatment (ie, in the setting of a positive culture) when a more narrow-spectrum agent could have been considered; and those used for an indication of surgical prophylaxis in the absence of infection when antimicrobials were not indicated for the procedure (eg, tunneled catheter placement), or if indicated, prescribed for a duration >24 hours postprocedure.[6] The following modifications from published guidelines were made. First, we considered antibiotic administration appropriate if coagulase-negative *Staphylococcus* was cultured from ≥1 blood culture (as opposed to ≥2 blood cultures) in the setting of fever, chills, or hypotension, given the high prevalence of bacteremia caused by this pathogen in the dialysis population. Second, we defined fever as a temperature >100°F, as opposed to the standard >100.4°F, because of the immunosuppressive state of CHD patients.[6] Medication allergies and drug-drug interactions were considered when assessing appropriateness. The appropriateness of the duration of therapy was not assessed.

Statistical analyses

Two analyses were performed: the first analysis characterized variables associated with antimicrobial receipt, and the second analysis characterized variables associated with inappropriately indicated antimicrobial doses. Nominal and ordinal variables were dichotomized or categorized in a clinically relevant manner. The number of hospitalizations in the preceding 12 months was categorized into no hospitalizations, 1-2 hospitalizations, or ≥3 hospitalizations based on the pattern of inpatient hospital use seen in clinical practice. Charlson Comorbidity Index score, a non-normally distributed continuous variable with a small range of values, was dichotomized around the median value.

In the first analysis, all patients who received at least 1 session of CHD during the study period were stratified into those receiving ≥1 parenteral antimicrobials and those who received no parenteral antimicrobials. Modeling was performed using multivariable logistic regression. Bivariate analyses of predictor variables potentially associated with antimicrobial receipt were performed using Fisher exact test for binary predictors, Pearson χ^2 test for nominal categorical predictors, and *t* test or Wilcoxon rank-sum test for continuous predictors. Variables with a 2-sided *P* value ≤ .20 were considered for the multivariable regression model. Nominal categorical variables were considered significant if ≥1 of the dummy-coded variables demonstrated significance ($P \leq .20$). A forward stepwise selection procedure was used to select variables for the final model. Statistical significance in the final model was defined as $P \leq .05$. Variables with a *P* value ≤.20 on bivariate analysis but not included in the stepwise selection model were added back to the model serially to assess for confounding. A variable was considered a confounder and included in the model if the β coefficient of any of the model variables changed by ≥20% with the addition of the confounding variable. Collinearity was assessed by removing the model variables serially, and each variable was considered for exclusion if the SEM of the effect estimates of the remaining model variables decreased by ≥20%. Effect modification was explored among clinically relevant variables through the use of interaction terms.

For the second analysis, the number of inappropriately indicated doses and observation time were tallied for each patient. Because the outcome for this analysis is overdispersed count data (inappropriately indicated antimicrobial doses received among study patients), modeling was performed using negative binomial regression. Bivariate analyses were conducted in the same manner as described for the first analysis. Variables with a *P* value ≤.20 on bivariate analysis were included in the final multivariable model without further selection procedures.

All data were collected and tabulated with a relational database (Microsoft Access 2003; Microsoft, Redmond, WA). Statistical analyses were performed using STATA software (version 10.0; StataCorp, College Station, TX).