Impact of Empiric Piperacillin/Tazobactam Use on Nephrotoxicity in Patients with Gram-negative Bacteremia

Farbod Dehghani, Eunice Yoo, Carlos Alvarez, Andrew Faust, Ronald G Hall

1Texas Tech University Health Sciences Center, School of Pharmacy; 2Hospital of the University of Pennsylvania; 3Texas Health Medical Center

ABSTRACT

Objective: Nephrotoxicity has been associated with increased total body weight in patients receiving vancomycin for Gram-positive infections. We sought to determine if the association of nephrotoxicity and increased total body weight was unique to patients receiving vancomycin or if it was observed in a cohort of patients with gram-negative bacteremia as well.

Methods: This was a retrospective cohort study at Texas Health Presbyterian-Dallas of patients who were at least 18 years old with a positive blood culture growing Escherichia coli, Pseudomonas aeruginosa, Enterobacter sp., Klebsiella sp., Acinetobacter sp., and Stenotrophomonas maltophilia between 1/1/2008-8/31/2011. Patients were also required to receive at least 48 hours of empiric antimicrobial therapy. Patients were excluded if they had a polymicrobial infection, mix Gram-positive and Gram-negative infection, or recurrent episode of bacteremia. Adequate empiric antibiotic therapy was defined as one or more antimicrobial(s) to which the pathogen was susceptible to within 24 hours of obtaining a blood culture. Nephrotoxicity was defined as an increase of at least 0.5 mg/dL in the serum creatinine or a 50 percent or more increase from baseline for at least two consecutive days. Multivariable logistic regression analysis using variables identified by conceptual modeling and those found to be significant by univariable analysis was used to identify variables independently associated with nephrotoxicity.

Results: There were 323 patients in the cohort and 15% developed nephrotoxicity. The mean age was 72 years (72% were at least 65 years old), with 37% of patients having a cancer diagnosis and 22% residing in the ICU when their gram-negative bacteremia was identified. Appropriate empiric therapy was received by 5% of patients. Total body weight ranged from 38.6 to 204.1 kg (mean 77.6 kg). Factors associated with nephrotoxicity included: ICU residence (Odds Ratio [OR] 2.23; 95% CI 1.38-3.57), total body weight greater than 80 kg (OR 3.17; 95% CI 1.65-6.01), and vasopressor use (OR 4.78; 95% CI 2.44-9.39). Baseline serum creatinine > 1.20 mg/dL was not associated with nephrotoxicity with piperacillin/tazobactam.

Nephrotoxicity occurred in 15% of our cohort of patients with gram-negative bacteremia. Empiric use of piperacillin/tazobactam was not associated with nephrotoxicity in our cohort. Empiric piperacillin/tazobactam was independently associated with an increased risk of nephrotoxicity if the baseline serum creatinine was greater than 2 mg/dL and vasopressor use was greater than 10.12 mg/kg.

CONCLUSION

This study has evaluated the impact of empiric piperacillin/tazobactam use on nephrotoxicity in patients with gram-negative bacteremia. Our findings results confirm review due to the single center nature of the study. An increased sample size will allow for additional potential confounders to be evaluated in the multivariable model.

FD, ET, CA, AF: Nothing to disclose; RHG: Genetech (Advisory board)

METHODS

Study design: A retrospective cohort study of patients ages 18 years old or older with gram-negative bacteremia who received at least 48 hours of empiric antimicrobial therapy was compiled between January 1, 2008-August 31, 2011. All patients had a positive blood culture growing 1 species of one of the pre-selected gram negative bacteria which included: E. coli, Pseudomonas aeruginosa, Enterobacter, Klebsiella, Acinetobacter, and Stenotrophomonas maltophilia. Patients with poly-microbial infections or mixed gram positive and gram negative infections were excluded. Recent episodes of bacteremia were excluded as well. The primary outcome was to determine if empiric use of piperacillin/tazobactam was associated with a higher nephrotoxicity rate.

Definitions: Nephrotoxicity: An increase of at least 0.5 mg/dL or a 50 percent or more increase from baseline for at least two consecutive days.

Adequate empiric antibiotic therapy: As at least one antimicrobial agent to which the pathogen was susceptible to within 24 hours of obtaining a blood culture.

Statistical analysis: All analysis were performed in Stata 14.0 (StataCorp LP, College Station, TX). Nominal variables were analyzed using a chi-square or Fisher's exact test as appropriate. Continuous and ordinal data were analyzed using a Wilcoxon Rank Sum test. Multivariable stepwise logistic regression analysis was performed with variables identified by conceptual modeling and those found to be significant by univariable analysis.

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DISCLOSURE

LIMITATIONS

Table 1: Participant characteristics (median)

Table 2: Univariable analysis of nephrotoxicity

Table 3: Multivariable analysis of nephrotoxicity

RESULTS

Our study evaluated the impact of empiric piperacillin/tazobactam use on nephrotoxicity in patients with gram-negative bacteremia. Our findings results confirm review due to the single center nature of the study. An increased sample size will allow for additional potential confounders to be evaluated in the multivariable model.