BACKGROUND

- Inhaled aminoglycosides serve as an attractive mode of therapy for the treatment and prevention of pulmonary infections in patients with cystic fibrosis, non-cystic fibrosis bronchiectasis, nontuberculous mycobacterial infections, or hospital-acquired pneumonia. Clinical practice guidelines support the use of inhaled tobramycin for chronic pseudomonas aeruginosa infection in patients with cystic fibrosis and chronic stable lung disease.

- Inhaled aminoglycosides achieve higher concentrations in lung tissue and minimize systemic exposure compared to intravenous systemic concentrations. Experimental models have shown that lung physiology and stage of infection may also affect permeability and absorption; in particular, damaged lung tissue may lend to elevated systemic concentrations.

- Aerosol drug delivery variations have been linked to variable drug absorption; in particular, damaged lung tissue may lend to elevated systemic drug levels while receiving an inhaled aminoglycoside. Numerous cases of nephrotoxicity and ototoxicity with inhaled aminoglycosides have been reported.

OBJECTIVES

Primary Objectives
- To perform an exploratory data analysis to identify risk factors associated with systemic drug levels while receiving an inhaled aminoglycoside

Secondary Objectives
- To determine if medication type (inhaled amikacin or inhaled tobramycin) and aminoglycoside drug level are associated with nephrotoxicity
- To determine if acute kidney injury or ototoxicity are associated with systemic drug levels while receiving an inhaled aminoglycoside
- To determine if concomitant nephrotoxic medications (nebulizer) and acute kidney injury, ototoxicity will be compared using Fisher exact or chi-square test

METHODS

Study Design
- IRB approved, retrospective, single-center, chart review
- Cohort study of inhaled amikacin and inhaled tobramycin
- Patients with a detectable drug level (≥ 0.5 mcg/mL)
- Patients with an undetectable drug level (< 0.5 mcg/mL)
- Unique patients meeting criteria with a detectable drug level between January 1, 2009 and July 1, 2015 will be included. An equal number of subjects with an undetectable level will be selected from a randomized list. Eligible subjects will be identified via query of the Duke Unified Content Explorer (DEDUCE) database

Data Analysis
- Multivariate Risk Assessment
  - Age
  - Body mass index
  - Charlson Comorbidity Index
  - Intensive care unit status
  - Diagnosis of active pneumonia
  - Consecutive duration of inhaled aminoglycoside
  - Lung transplant recipient
  - Presence of chronic kidney disease stage III-V
  - Acute kidney injury
- Multivariate Risk Assessment
  - Secondary outcomes of incidence of nephrotoxicity and incidence of ototoxicity will be compared using Fisher exact or chi-square test
- A logistic regression model will be used to assess the relationship between aminoglycoside type, drug level, and acute kidney injury, adjusting for covariate risk factors (age, presence of chronic kidney disease stage III-V, elevated Charlson Comorbidity Index, and concomitant nephrotropic medications)

Inclusion Criteria
- Age ≥ 18 years
- Receipt of at least one dose of an inhaled aminoglycoside during inpatient hospitalization with a drug level drawn within 6 hours prior to next dose

Exclusion Criteria
- Receipt of an intravenous aminoglycoside within 96 hours
- Receipt of at least one dose of an inhaled aminoglycoside

REFERENCES