Retrospective Comparison of the Incidence of Acute Kidney Injury in Patients Treated with Intravenous Polymyxin B or Intravenous Colistimethate Sodium

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Purpose

This study will evaluate and compare the incidence of acute kidney injury among patients treated with intravenous polymyxin B and intravenous colistimethate sodium. In a secondary analysis, risk factors that may contribute to the development of acute kidney injury in each group will be evaluated.

Background

- The polymyxin drug class is effective against Gram-negative bacteria including *Pseudomonas aeruginosa, Acinetobacter baumannii and Klebsiella pneumoniae.*
- The polymyxins as antimicrobial therapy had previously been replaced by more effective, less toxic agents. The emergence of multidrug-resistant bacterium has prompted their utilization in clinical practice.[1]
- Colistin is available in two forms, the pro-drug colistimethate sodium and its active, more toxic form, colistin sulfate. Conversion of colistimethate sodium to colistin is required for antimicrobial activity since colistimethate sodium itself is inactive. Colistimethate sodium is the only formulation currently available in the United States.[2]
- The Risk, Injury, Failure, Loss, End-Stage (RIFLE) criterion defines three severity grades for acute kidney injury (risk, injury, failure) and two outcomes (loss and end-stage). Grading of renal dysfunction is classified by a change in serum creatinine or glomerular filtration rate.[3]
- The incidence of acute kidney injury with colistimethate sodium is variable, ranging from 0%-37%.[4] Recent studies utilizing the RIFLE criteria report incidences as high as 31%-53.5%.[5,6,7]
- The incidence of acute kidney injury associated with polymyxin B ranges widely from 6%-54%.[4] A recent study reported an incidence of 60% through utilization of the RIFLE criteria.[8]
- Risk factors for the development of kidney injury with polymyxin therapy may include treatment duration greater than 14 days, higher total cumulative drug exposure, use of concomitant nephrotoxic agents and presence of co-morbidities including chronic kidney diseae and hypertension.

Study Design

Retrospective chart review of 150 patients in each group receiving intravenous polymyxin B or intravenous colistimethate sodium for at least 48 hours for all Gram-negative bacterial infections.

Study Population

- Inclusion Criteria:
  - Patients over 18 years of age administered either agent during the course of hospital stay for any type of Gram-negative infection.
- Exclusion Criteria:
  - Diagnosis of end-stage renal disease or a dialysis candidate prior to therapy initiation, known hypersensitivity to polymyxin B or colistimethate sodium, less than 48 hours of polymyxin therapy, previous exposure to polymyxin therapy at any point during the specified study period and use of inhalational colistimethate sodium monotherapy.

Methods

- The primary outcome is to compare the incidence of acute kidney injury in patients administered intravenous polymyxin B to patients administered intravenous colistimethate sodium.
  - Acute kidney injury will be defined by use of the RIFLE criteria measured by change in serum creatinine.
- A secondary analysis will be performed based on patient demographics in each group to evaluate risk factors that may be predictors in the development of acute kidney injury.
- Patient data to be collected will include:
  - Age, weight at therapy initiation, gender, APACHE II score and co-morbid disease states (chronic kidney disease, diabetes mellitus, hypertension).
  - Baseline and serial serum creatinine, actual body weight-based daily dose, cumulative dose and duration of treatment.
  - Use and duration of concomitant nephrotoxic agents (vancomycin, aminoglycosides, vasopressors, amphotericin B, angiotensin converting enzyme inhibitors, angiotensin receptor blockers, calcineurin inhibitors, non-steroidal anti-inflammatory drugs, ganciclovir, IV contrast medium).
- Following data collection, the rate of acute kidney injury in each group will be determined and compared for significance utilizing the chi-squared test.

Disclosure

Authors of the presentation have the following to disclose concerning possible financial or personal relationships with commercial entities that may have a direct or indirect interest in the subject matter of this presentation.

- Rebecca Sumner-Nothing to disclose
- Jarrod Kile- Nothing to disclose

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