Colistin Versus Optimized Polymyxin B: Impact on Nephrotoxicity

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Background

- Polymyxins B and E (colistin) have rejoined the antibiotic armamentarium due to a dramatic increase in multidrug-resistant (MDR) bacteria.[1]
- Although structurally very similar, polymyxin B and colistin are not clinically interchangeable.

COLISTIN[2]

- Intravenous colistin is formulated as colistimethate (CMS), an inactive prodrug.
- In patients with normal renal function, only ~20-25% of the original CMS dose is converted to active drug before being cleared renally.
- Due to interpatient variability in metabolism, up to 10-fold differences in colistin plasma concentrations have been observed following administration of equivalent doses.
- Carilion Clinic implemented optimized colistin dosing based on recent study data, instead of traditional, weight-based colistin dosing, for urinary tract infections.

POLYMYXIN B

- Polymyxin B is administered in its active form and undergoes nonrenal clearance.[2]
- There is little interpatient variability in metabolism and the relationship between dose and serum level is much more predictable than that with colistin.[2]
- The polymyxin B doses required to overcome the increasing minimum inhibitory concentrations (MICs) of resistant organisms are higher than those described in the original package labelling.[1]
- A recent pharmacokinetic study recommended more aggressive dosing based on total body weight instead of renal function.[3]
- In September 2013, Carilion Clinic began utilizing high-dose polymyxin B for infections by MDR organisms (MDROs) outside of the urinary tract.

Study Objectives

PRIMARY

- Describe the rates of nephrotoxicity associated with colistin and weight-based polymyxin B administration

SECONDARY

- Characterize neurotoxicity and mortality associated with colistin and polymyxin B

Methods

STUDY DESIGN

- This was a retrospective, single-center cohort study.
- The study protocol was deemed exempt by the Carilion Clinic Institutional Review Board.

SETTING AND POPULATION

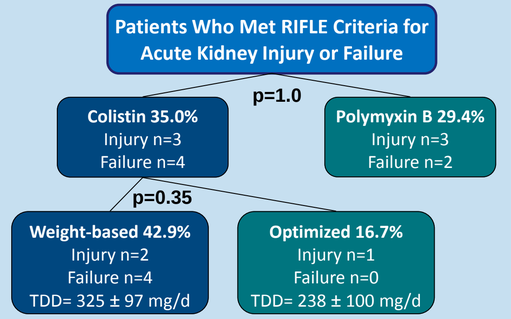
- Conducted at Carilion Clinic Roanoke Memorial Hospital, a 763 - bed tertiary care facility located in Roanoke, VA.
- Adult patients who received intravenous colistin or polymyxin B at any Carilion Clinic inpatient facility between January 2010 and June 2015 were included in this study.

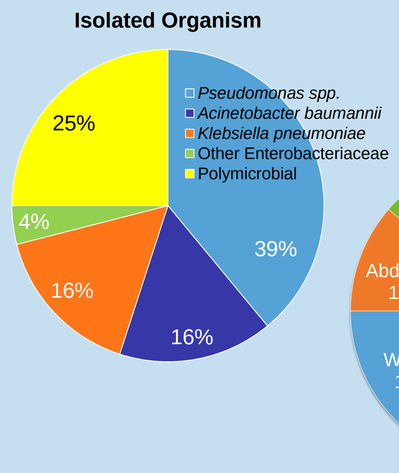
DATA COLLECTION

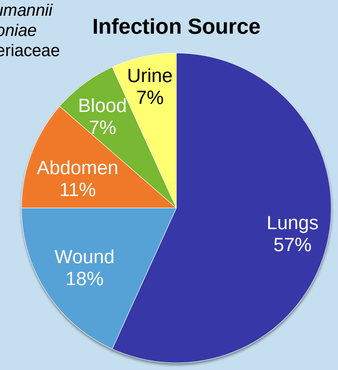
- Data were extracted from the Epic electronic medical record using a standardized data collection tool.

Results

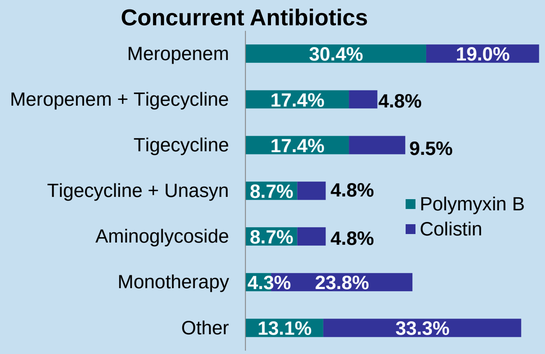
Baseline Patient Characteristics	Polymyxin B (n=20)	Colistin (n=17)
Age, years (mean ± SD)	52.1 ± 14.4	53.2 ± 17.2
Female gender, n (%)	10 (43.5)	9 (39.1)
TBW, kg (mean ± SD)	99.6 ± 38.2	97.4 ± 38.4
Duration of therapy, days (mean ± SD)	8.9 ± 10.3	7.4 ± 6.1
Baseline creatinine, mg/dL (mean ± SD)	0.81 ± 0.44	0.92 ± 0.87
Risk Factors for Nephrotoxicity		
Hypertension, n (%)	12 (52.2)	11 (52.4)
Diabetes mellitus, n (%)	10 (43.5)	11 (52.4)
Concurrent nephrotoxins, n (mean ± SD)	1.3 ± 1.2	1.3 ± 1.2
Modified Acute Physiology Score (mean ± SD)	31.4 ± 15.3	34.9 ± 12.6







Secondary Outcomes, n (%)	Polymyxin B	Colistin
Neurotoxicity	3 (13.0)	2 (9.5)
Mortality	8 (34.8)	8 (38.1)



Summary

- There were no significant differences in study patients at baseline, including risk factors for nephrotoxicity.
- No statistically significant differences in the rates of nephrotoxicity, neurotoxicity, or mortality in patients receiving polymyxin B versus colistin were observed.
  - There appears to be a clinically significant increase in rates of acute kidney injury and failure in patients who received weight-based colistin.
  - The reported neurotoxicities attributed to polymyxin B or colistin administration were peripheral paresthesia (n=2), oral paresthesia (n=1), dizziness (n=1), and delirium (n=1).
- Despite evaluating all patients who received a polymyxin over a 5-year period, the study population was small and the study itself was not designed to assess outcomes.
- Based on this data, Carilion Clinic will continue to utilize aggressive, weight-based polymyxin dosing for MDROs as no differences in toxicity were demonstrated.
- Further study is needed to evaluate differences in infection outcomes and mortality.

References

1. Li J, Nation RL, Owen RJ, et al. Antibiograms of multidrug-resistant clinical *Acinetobacter baumannii*: promising therapeutic options for treatment of infection with colistin-resistant strains. *Clin Infect Dis.* 2007;45(5):594-8.
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3. Sandri AM, Landersdorfer CB, Jacob J, et al. Population pharmacokinetics of intravenous polymyxin B in critically ill patients: implications for selection of dosage regimens. *Clin Infect Dis*. 2013;57(4):524-31.

Disclosure: Authors of this 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:

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