# Systemic Administration of Polymyxin B in Renal Transplant Recipients with Multidrug-Resistant Infections and Its Associated Nephrotoxicity

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## Abstract

**Objective:** Infection with multidrug-resistant organism (MDRO) is an important issue for hospitalized patients, but of great concern for renal transplant recipients whom are associated with high mortality and morbidity. Historically, polymyxin B has been shown to be up to 50% nephrotoxic and its use in renal transplant recipients would be avoided. However, infections with MDRO have limited therapeutic options, requiring the use of last-line agents such as polymyxin B. Our clinical experience with systemic polymyxin B in renal transplant recipients with MDR infections is limited and needs to be explored.
**Methods:** Retrospective chart reviews were conducted for adult renal transplant recipients who received parenteral polymyxin B ≥ 48 hours for MDRO infection. Patient characteristics, infection type, causative organism, polymyxin B dose/frequency/duration, renal function throughout polymyxin B therapy, and concomitant use of nephrotoxic agents (aminoglycosides, sulfonamides, non-steroidal anti-inflammatory drugs, etc) were collected. Nephrotoxicity was defined as a rise in serum creatinine ≥ 0.5 mg/dL or a ≥ 50% reduction in creatinine clearance from baseline. Clinical/microbiological outcomes and mortality were also evaluated.
**Results:** A total of 35 renal transplant recipients were identified, retrospective chart review were conducted for 19 non-hemodialysis patients who received IV polymyxin B > 48 hours ( 74% maile, mean age of 63 years old). Common infections were bacteremia (31%), UTI (30%), and pneumonia (13%). Common organisms were *K. pneumoniae* (53%), *A, baumanii* (18%) and *E, coli* (17%). Patients had a mean CrCl of 60 mL/min prior to polymyxin B administration. Mean duration of polymyxin B therapy was 8 days. Nephrotoxicity occurred in 47% of patients and on average by day 6 of polymyxin B therapy, however, 78% of those patients also received at least one nephrotoxic drug. No patients experienced acute rejection episodes. Microbiological clearance was achieved in 68% of patients. Two patients died before discharge and five more died within 30 days of receiving polymyxin B for various reasons.
**Conclusions:** Polymyxin B nephrotoxicity was 47% in renal transplant recipients. Given that most of the episodes of nephrotoxicity were associated with concomitant nephrotoxic drugs, true polymyxin B nephrotoxicity rate is lower. Further studies would need to be done to more rigorously assess its value in renal transplant recipients.

## Background

- Polymyxin B (PB) is a cationic detergents that binds to bacterial membrane phospholipids, altering permeability and resulting in leakage of intracellular contents[1-3]
- Nephrotoxicity associated with PB occurs as a result of increased membrane permeability of renal epithelial cells
- Older literature reports nephrotoxicity rates of 36%-50%,[4] but recent literature reports lower incidence of toxicity closer to 14%[5]
- Resistance is an emergent issue for hospitalized patients, especially in renal transplant recipients (RTR) where infection is a leading cause of mortality[6]
- With emergence of multidrug-resistant organism (MDRO), PB becomes a treatment of last resort for these infections. Use of PB in RTR is especially concerning given its potential for nephrotoxicity"

## Objective

The purpose of the study is to review our clinical experience with systemic PB in RTR with MDRO infections, focusing on microbiological outcomes and nephrotoxicity.

## Methods

- Medical records of adult RTR who received IV PB ≥ 48 hours between 2006-2011 for MDRO infections were reviewed for the following:
  - Baseline demographics
    - Gender, race, age, weight, co-morbidities, creatinine clearance (CrCl, calculated by Cockcroft Gault equation), infection type, causative organism, PB regimen, concomitant nephrotoxic medications excluding baseline cyclosporine and tacrolimus
  - Clinical lab values
    - Serum creatinine (SCr) before, during, and after IV PB use
  - Outcome data
    - Nephrotoxicity (rise in Scr ≥ 0.5 mg/dL or a ≥ 50% reduction in CrCl from baseline), microbiological cure, clinical cure, and survival to discharge and 30 days

## Results

**Figure 1. Patient Inclusion and Exclusion Criteria Flowchart**

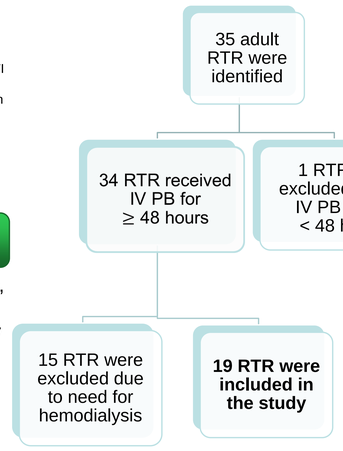


**Table 1. Baseline Patient Characteristics**

| Parameter | N = 19 |
|---|---|
| **Male sex, n (%)** | 14 (74) |
| **Race** | |
| White | 4 (21) |
| Black | 6 (32) |
| Hispanic | 8 (42) |
| Asian | 1 (5) |
| **Age, mean ± SD in years** | 63 ± 10 |
| **Weight, mean ± SD in kg** | 81 ± 19 |
| **Co-morbidities, n (%)** | |
| Hypertension | 15 (79) |
| Diabetes | 11 (58) |
| Hyperlipidemia | 7 (37) |
| Malignancy | 1 (5) |
| HIV | 1 (5) |
| **CrCl (prior to IV PB), mean ± SD in mL/min** | 60 ± 51 |
| **Duration of treatment, mean ± SD in days** | 8 ± 6 |

**Figure 2. Type of Infection**

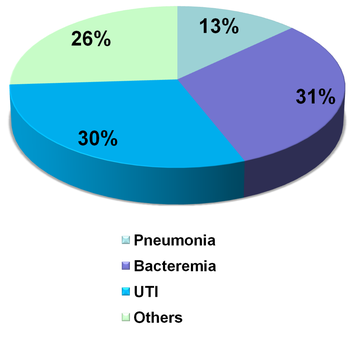


**Figure 3. Organisms**

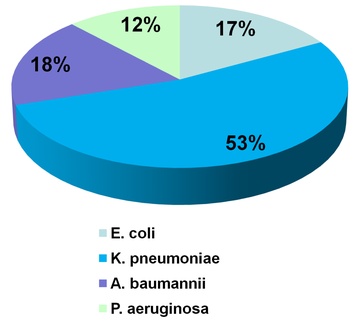


**Table 2. Nephrotoxicity and Clinical/Microbiological Outcomes**

| Parameter | N = 19 |
|---|---|
| **Nephrotoxicity, n (%)** | 9 (47) |
| Concomitant nephrotoxic medications (Aminoglycoside, NSAIDs, etc.), n (%) | 7 (78) |
| Time to event, mean ± SD in days | 6 ± 3 |
| SCr at event, mean ± SD in mg/dL | 2.7 ± 1.04 |
| CrCl at event, mean ± SD in mL/min | 35 ± 17.9 |
| Number of patient developed acute rejection or on HD | 0 |
| **IV PB dose, mean ± SD in units/kg/day** | 13,390 ± 6481 |
| **Microbiological cure, n (%)** | 13 (68) |
| **Clinical cure, n (%)** | 13 (68) |
| **Survival, n (%)** | |
| At discharge | 17 (89) |
| At day 30 after IV PB | 12 (63) |

## Limitations

- Retrospective chart review
- Small sample size
- No control group
- Confounding factors: most patients were on concomitant nephortoxins while on PB

## Conclusions

- Nephrotoxicity occurred in 9 out of 19 (47%) patients and on average by day 6 of PB therapy
- Of those who developed nephrotoxicity, 7 out of 9 (78%) received at least one concomitant nephrotoxic medication while on PB
- Despite nephrotoxicity, no patients required hemodialysis or developed acute rejection
- True nephrotoxicity of PB might be lower, larger studies are needed to assess nephrotoxicity of PB in RTR

## References

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