Effectiveness and Safety of Polymyxin B for Infections Caused by Extensively Drug-Resistant Gram-Negative Bacteria in Thailand

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Background and Objectives

Colistimethate sodium, inactive prodrug of colistin, has been used for therapy of infections caused by extensively drug-resistant (XDR) Gram-negative bacteria over the past 10 years with mortality of 15% to 60% and nephrotoxicity of 10% to 60%. Polymyxin B may have several advantages over colistin including it is an active drug, it is somewhat more active than colistin, adjustment of the dose may not be needed for the patient with impaired renal function, and it may have less nephrotoxicity.

The objective of this multicenter study was to determine the effectiveness and safety of polymyxin B for the treatment of XDR Gram-negative bacterial infections in Thai patients.

Patients and Methods

Adult patients hospitalized at 4 participating tertiary care hospitals during January and December 2015 who had infections caused by XDR Gram-negative bacteria were enrolled in the study.

Polymyxin B was usually given intravenously every 12 hours at the dosage of 100 mg per day for 7 to 14 days without dose adjustment for the patients' renal function. The primary outcomes were clinical response at the end of polymyxin B therapy and all cause 28-day mortality whereas the secondary outcomes were microbiological clearance of the target XDR bacteria and adverse drug reactions.

Table 1. Baseline characteristics

	N (%)
Male	40 (54.8%)
Mean age, years ± SD, (range)	59.8 ± 15.6 (20-80)
Mean body mass index (kg/m^2) ± SD, (range)	21.3 ± 4 (13-30)
Previous antibacterial agents exposure	70 (95.9%)
- Carbapenems	53 (40.2%)
- Beta-lactamase Inhibitor	26 (19.7%)
- Others	32 (24.2%)

Table 3. Treatment outcomes

	N (%)
Good clinical response	57 (78.1%)
All cause 28-day mortality	21 (28.7%)
Microbiological clearance	41 (56.2%)
Nephrotoxicity	18 (24.7%)
Neurotoxicity	2 (2.8%)

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Results

73 patients received polymyxin B for treatment XDR Gram-negative bacterial infections longer than 48 hrs were included. The baseline characteristics of the patients are shown in **Table 1**. Nearly all patients received antibacterial agents, including carbapenems, within the preceding 14 days of study enrollment.

The clinical characteristics of the patients are shown in **Table 2**. The patients received intravenous polymyxin B at a mean dosage of 1.9 mg/kg/day with a mean (range) duration of treatment of 11.7 (4 to 14) days. Pneumonia was the most common type of infections (60.3%), followed by tracheobronchitis (20.5%) and blood stream infection (15.1%). *A. baumannii* was the most common causative bacteria (51.5%) and all strains were susceptible to colistin.

Treatment outcomes are shown in **Table 3**. Good clinical response at the end of treatment was observed in 78.1% of the patients. All cause 28-day mortality was 28.7%. Microbiological eradication of the target bacteria at the end of therapy was 56.2%. Nephrotoxicity was observed in 18 patients (24.7%) in whom four patients (5.5%) required renal replacement. Only 2 patients (2.8%) had reversible numbness.

Conclusions

Polymyxin B appears to be effective and safe for treatment of infections caused by XDR gram-negative bacteria in Thai adult patients. Nephrotoxicity related to polymyxin B seems to be lower than that of colistin reported in other case series in Thai patients. Polymyxin B should be considered as an effective alternative therapy of infections caused by XDR gram-negative bacteria especially in the patients at risk of nephrotoxicity.

Table 2. Clinical characteristics

Mean APACHE II ± SD (range)	19.5 ± 6.9 (2-42)
Mean dosage (mg/kg/day)±SD	1.9 ± 0.3
Mean treatment duration ± SD (days)	11.7 ± 3.2
Types of infection	**N (%)**
- Pneumonia	44 (60.3%)
- Tracheobronchitis	15 (20.5%)
- Bloodstream infection	11 (15.1%)
- Others	7 (9.5%)
Causative Bacteria	**N (%)**
-*Acinetobacter baumannii*	69 (51.5%)
-*Pseudomonas aeruginosa*	33 (24.6%)
-*Klebsiella pneumoniae*	11 (8.2%)
-Others	10 (7.5%)
Concomitant antimicrobial agents*	53 (72.6%)
-Carbapenems	16 (22.5%)
-Levofloxacin	10 (14.1%)
-Vancomycin	9 (12.7%)
-Others	22 (30.9%)

* One patient could receive more than one agents