Monitoring of Effectiveness and Safety of Colistin for Therapy in Resistant Gram-Negative Bacterial Infections in Hospitalized Patients at Siriraj Hospital

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Objective: *To monitor the effectiveness and safety of colistin for therapy in resistant Gram-negative bacterial infections at Siriraj Hospital 10 years after colistin was first introduced in Thailand at Siriraj Hospital in 2005.*
Material and Method: *Study subjects were hospitalized adult patients with documented Gram-negative bacterial infections that received parenteral colistin (Colistate®) for longer than 48 hours between October 2014 and June 2015. Patient information regarding demographics, characteristics of infections, antibiotic therapy, clinical outcomes, microbiological responses, and nephrotoxicity were identified and retrieved from patient medical records. The data were analyzed using descriptive statistics.*
Results: *One hundred thirty eight patients were included in the study. Many of the patients were elderly males. The most common type of infection was pneumonia and A. baumannii was the most common cause of infection. Nearly all isolates of A. baumannii and P. aeruginosa were resistant to carbapenems. A loading dose of colistin (300 mg) was given in 94.9% of patients. Only 19.6% of patients received colistin alone. Most patients received concomitant antibiotics, especially carbapenems, and piperacillin-tazobactam. Favorable clinical outcome was observed in 71.7% of patients at the end of colistin therapy. Patient mortality at the end of colistin therapy and at 30 days after colistin therapy was completed was 23.2% and 39.9%, respectively. Microbiological eradication of target bacteria at the end of colistin therapy was found in 50.0% of patients. Overall incidence of acute kidney injury was 39.9%, with most cases classified as either risk (20.3%) or injury (13%). Colistin-related renal dysfunction was reversible in most cases.*
Conclusion: *Colistin remains the principal antibiotic in carbapenem-resistant Gram-negative bacterial infections. Colistin's effectiveness and safety is still rated as moderate for therapy in difficult-to-treat resistant Gram-negative bacterial infections.*

Keywords: *Colistin, Effectiveness, Gram-negative bacterial infections, Safety*

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Healthcare-associated infections (HAIs) are prevalent in regional and tertiary referral hospitals in Thailand and Gram-negative bacteria, including *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, and *Klebsiella pneumoniae*, are the most common causes of these infections[1]. Pneumonia is the most common type of healthcare-associated infection. *A. baumannii* is the most common cause of healthcare-associated pneumonia, followed by *P. aeruginosa*, and *K. pneumoniae*[1-4]. Carbapenem resistance was observed in 82%, 23%, and 1% of *A. baumannii*, *P. aeruginosa*, and *K. pneumoniae* isolated from patients with healthcare-acquired pneumonia in Thailand, respectively[2]. Higher mortality in healthcare-acquired pneumonia was observed in patients who received discordant antibiotics[2]. Polymyxins (colistin or polymyxin E and polymyxin B) have been reintroduced for therapy in multidrug-resistant Gram-negative bacterial infections, especially those caused by carbapenem-resistant Gram-negative bacteria over the past decade[5]. Colistin is administered parenterally as colistimethate sodium, an inactive pro-drug that is converted to colistin, which is the pharmacologic entity that possesses both antibacterial activity and the potential to cause toxicity[6,7]. Treatment of carbapenem-resistant Gram-negative bacterial infections with colistin that was locally manufactured at Siriraj Hospital between 2005 and 2006 resulted in a 46% 30-day mortality rate vs. an 80% 30-day mortality rate in patients who received other antibiotics[8]. Population

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pharmacokinetic analysis of colistimethate sodium and formed colistin in critically-ill patients revealed that a loading dose of colistin and maintenance doses of colistin were necessary to achieve an average colistin concentration at a steady state of 2.5 mg/l[9]. Pharmacokinetic analysis of colistimethate sodium and formed colistin in 170 critically ill patients at Siriraj Hospital was used to formulate the colistin dosing regimens that have been used at Siriraj Hospital and all over Thailand since 2012 (Table 1).

The objective of the study was to monitor the effectiveness and safety of colistin for therapy in resistant Gram-negative bacterial infections at Siriraj Hospital at 10 years after colistin was first introduced in Thailand at Siriraj Hospital in 2005.

Material and Method

The protocol for this study was reviewed and approved by the Siriraj Institutional Review Board. Study subjects were consecutive hospitalized adult patients (aged ≥18 years) with documented Gram-negative bacterial infections who received parenteral colistin (Colistate®) for longer than two days between October 2014 and June 2015 study period. Patient information regarding demographics, characteristics of infections, antibiotic therapy, clinical outcomes, microbiological responses, and acute kidney injury of eligible study subjects were identified and retrieved from medical records. Clinical outcomes at the end of colistin treatment were classified as favorable outcome (absence or improvement in signs and symptoms attributable to target infections) or non-favorable outcome (persistence or progression of disease or death). Microbiological responses at the end of treatment were classified as eradication (no target bacteria were found), persistence (target bacteria were still recovered), new infection (presence of new infection due to other organisms), or undetermined (clinical specimens were unavailable for culture). RIFLE classification was used to grade acute kidney injury, as follows: risk: serum creatinine increase of 1.5 times baseline or glomerular filtration rate (GFR) decrease >25%; injury: serum creatinine increase of two times baseline or GFR decrease >50%; failure: serum creatinine increase of three times baseline or GFR decrease >75%; loss of kidney function: complete loss of renal function for more than four weeks; and end-stage kidney disease: complete loss of renal function for more than three months[10]. The data were analyzed using descriptive statistics.

Table 1. Colistin dosing regimens based on pharmacokinetics of colistin in critically-ill Thai patients

Creatinine clearance* (ml/minute)	Suggested colistin (colistin-based activity) dose	
	Loading dose	Maintenance dose
>50	300 mg	150 mg q 12 h or 100 mg q 8 h
41-50	300 mg	150 mg q 12 h or 75-100 mg q 8 h
31-40	300 mg	75-100 mg q 12 h
21-30	300 mg	75 mg q 12 h or 150 mg q 24 h
11-20	300 mg	100 mg q 24 h
≤10	150 mg	75 mg q 24 h

* Cockcroft-Gault equation

Results

One hundred thirty eight patients met the eligibility criteria. Patient demographics, underlying conditions, type of hospitalization, use of antibiotics prior to receiving colistin, site of infections, causative bacteria, and colistin therapy are shown in Table 2. A disproportionate percentage of patients were elderly males. All patients had underlying conditions, especially chronic or severe conditions.

Mean (SD) APACHE II score at initiation of colistin was 21.7 (7.7) in 65 patients for whom there was sufficient data for calculation of the score. Many patients developed resistant Gram-negative bacterial infections while they were hospitalized in general wards. Most patients were put on mechanical ventilators at time of initiation of colistin therapy. All patients received antibiotics prior to initiation of colistin therapy. Anti-Gram negative antibiotics that were commonly prescribed prior to initiation of colistin were ceftriaxone, ceftazidime, piperacillin-tazobactam, meropenem, imipenem, ciprofloxacin, and amikacin. The most common type of infection was pneumonia, followed by tracheobronchitis, urinary tract infection, intra-abdominal infection, bacteremia, and skin and soft tissue infection. *A. baumannii* was the most common cause of infections, followed by *P. aeruginosa*, and Enterobacteriaceae. Some patients had mixed bacteria isolated from the site of infection, such as mixed resistant Gram-negative bacteria or mixed resistant Gram-negative bacteria and *Staphylococcus aureus*. Nearly all isolates of *A. baumannii* and *P. aeruginosa* were resistant to carbapenems. Most of Enterobacteriaceae were extended-spectrum beta-lactamase (ESBL) producing strains. Two isolates of

Table 2. Characteristics of 138 adult patients with documented Gram-negative bacterial infection who received parenteral colistin (Colistate®) for longer than two days

Patient characteristics	Findings
Gender	
Male	77 (55.8%)
Female	61 (44.2%)
Age (years)	
Mean (SD)	68.4 (21.6)
Range	18-94
Underlying conditions*	
Diabetes mellitus	59 (42.8%)
Cardiovascular disease	41 (29.7%)
Malignancy	41 (29.7%)
Cerebrovascular disease	40 (29.0%)
Chronic lung disease	28 (20.3%)
Chronic kidney disease	21 (15.2%)
Chronic liver disease	19 (13.8%)
Post-major surgery	14 (10.1%)
Type of hospitalization when colistin was initiated	
Intensive care unit	64 (46.4%)
General ward	74 (53.6%)
Patient on mechanical ventilator when colistin was initiated	119 (86.2%)
Prior use of antibiotics before receiving colistin	138 (100%)
Site of infection*	
Pneumonia	71 (51.5%)
Tracheobronchitis	45 (32.6%)
Bacteremia	10 (7.2%)
Urinary tract infection	9 (6.5%)
Intra-abdominal infection	9 (6.5%)
Skin and soft tissue infection	5 (3.6%)
Causative bacteria*	
Acinetobacter baumannii	110 (79.7%)
Pseudomonas aeruginosa	31 (22.4%)
Enterobacteriaceae (*K. pneumoniae*, *Enterobacter* spp., *E. coli*)	31 (22.4%)
Colistin therapy	
Loading dose (300 mg)	131 (94.9%)
Mean duration of colistin (days), (SD)	9.4 (2.8)
Median duration of colistin (days)	7
Range of duration of colistin (days)	3-21
Mean dose of colistin per day (mg), (SD)	231 (45.4)
Median dose of colistin per day (mg)	200
Range of colistin dose per day (mg)	75-300
Concomitant nebulized colistin	3 (2.2%)
Concomitant antibiotic therapy*	
Carbapenem (meropenem, imipenem, doripenem)	69 (50.0%)
Piperacillin-tazobactam	28 (20.3%)
Cefoperazone-sulbactam	11 (8.0%)
Vancomycin	11 (8.0%)
Fosfomycin	10 (7.2%)
Fluoroquinolones (ciprofloxacin, levofloxacin)	10 (7.2%)
Others (metronidazole, clindamycin, ampicillin, tigecycline, co-amoxiclav, netilmicin, linezolid)	20 (14.5%)

Data presented as n (%), unless specified otherwise
* Individual patients can have more than one characteristic

K. pneumoniae were resistant to carbapenems. All isolates of *A. baumannii* and *P. aeruginosa* were susceptible to colistin. A 300 mg loading dose of colistin was given to 94.9% of patients. Mean and median daily doses of colistin were 231 mg and 200 mg, respectively, with a range of 75 mg to 300 mg. Mean and median durations of colistin were 9.4 and 7 days, respectively, with a range of 3 to 21 days. Only 19.6% of the patients received only colistin as anti-Gram negative therapy. Only 2.2% of patients received concomitant colistin inhalation. Most patients received concomitant antibiotics; most notably carbapenems and piperacillin-tazobactam.

Clinical outcomes, microbiological responses, and incidence of acute kidney injury at the end of colistin treatment and at 30 days after completion of colistin treatment are shown in Table 3. Favorable clinical outcome was observed in 71.7% of patients at the end of colistin therapy. Patient mortality was 23.2% at the end of colistin therapy, with infection being the cause of death in nearly all cases. Overall 30-day mortality was 39.9%. The increase in mortality from end of colistin therapy to 30 days after end of colistin therapy resulted from super-infections or their underlying conditions or complications relating to other underlying conditions. Microbiological responses at the end of colistin treatment were eradication, persistence, and new infections in 50.0%, 18.8%, and 13.0%, respectively. Overall incidence of acute kidney injury was 39.9%, of which 20.3%, 13.0%,

Table 3. Clinical outcomes, microbiological responses, and acute kidney injury at the end of colistin treatment in 138 patients

Outcome	Result
Clinical outcome at the end of colistin treatment	
Favorable outcome	99 (71.7%)
Non-favorable outcome	7 (5.1%)
Death	32 (23.2%)
Overall 30-day mortality	55 (39.9%)
Microbiological responses at the end of colistin treatment	
Eradication	69 (50.0%)
Persistence	26 (18.8%)
New infection	18 (13.0%)
Undetermined	25 (18.1%)
Acute kidney injury	
Overall	55 (39.9%)
Risk	28 (20.3%)
Injury	18 (13.0%)
Failure	9 (6.5%)

All data presented as n (%)

and 6.5% were risk, injury, and failure, respectively. Seven patients received hemodialysis due to progressive renal insufficiency and related complications. All patients with acute kidney injury who survived at 30 days after completion of colistin therapy had improved renal function and/or serum creatinine level had returned to baseline value. No serious neurotoxicity was documented in any of our patients.

Discussion

This study confirms that colistin is the principal therapy for infections in elderly patients who are critically ill with difficult-to-treat infections, like carbapenem-resistant *A. baumannii* hospital-acquired pneumonia. The key findings from this study regarding outcomes in patients with resistant Gram-negative severe infections treated with parenteral colistin were: 1) favorable clinical outcome at the end of colistin therapy was 71.7%, 2) overall mortality at the end of colistin therapy and at 30 days after completion of colistin therapy was 23.2% and 39.9%, respectively, 3) microbiological eradication of the target bacteria at the end of colistin therapy was 50.0%, and 4) incidence of acute kidney injury was 39.9%. Most of the patients with acute kidney injury were classified as either risk or injury and their impaired renal functions were usually reversible.

Many descriptive and cross-sectional studies regarding colistin treatment in carbapenem-resistant *A. baumannii* infections have been reported from Taiwan, Korea, Vietnam, and Thailand over the past five years[11-15]. Although these studies included many critically ill ICU patients with *A. baumannii* isolates, nearly all of which were susceptible to colistin (similar to the present study). It would be difficult to compare those findings with the results from our study. Differences between the aforementioned studies and the present study include study design, patient characteristics, hospital settings, colistin dosing regimens, concomitant antibiotic therapy, and modes of supportive care. It would also be difficult to compare the results of the study on colistin therapy in multidrug-resistant non-fermenters that was conducted at Siriraj Hospital between 2005 and 2006[8] with the results from the present study (2015). Patients in our study were older than in the previous study and we included tracheobronchitis, which was not included in the 2005-2006 study. A loading dose of colistin was given to nearly all patients in our study, whereas the patients in the previous Siriraj study did not receive a loading dose of colistin. Most patients in our study (80.4%) received colistin combined with other antibiotics, whereas only 58% of patients who were treated with colistin in the previous Siriraj study received other antibiotics. The present study also included only patients who received colistin longer than two days. Dosing protocols for parenteral colistin in severe resistant Gram-negative infections are normally based on locally produced evidence. Colistin dosing regimens, including a loading dose of colistin, that were administered to nearly all patients in our study were based on pharmacokinetic analysis of colistimethate sodium and formed colistin in 170 critically ill patients at Siriraj Hospital. Only three patients received nebulized colistin, because a randomized controlled trial of nebulized colistin as adjunctive therapy in ventilator-associated pneumonia caused by Gram-negative bacteria at Siriraj Hospital did not observe mortality benefit in patients who received nebulized colistin[16]. Regarding the use of colistin combined with other antibiotics for therapy in severe infections due to carbapenem-resistant non-fermenters, there has been no solid evidence from a well-conducted, large randomized controlled study demonstrating that colistin combined with other antibiotics is more beneficial than colistin monotherapy. A recent systematic review and meta-analysis of in vitro synergy of polymyxins with other antibiotics for treatment of *A. baumannii* revealed that in vitro synergy and bactericidal activity against carbapenem-resistant *A. baumannii* were found in polymyxins combined with several antibiotic classes, including carbapenems, glycopeptides, and rifampicin[17]. However, several clinical studies in treatment of carbapenem-resistant *A. baumannii* infections with colistin combined with rifampicin or vancomycin showed no clinical benefit when compared with colistin monotherapy[18,19]. The efficacy of colistin combined with carbapenem for therapy in carbapenem-resistant *A. baumannii* infections from non-randomized controlled studies remains inconclusive[20-22]. Results from two multicenter, multinational randomized controlled studies that are currently being conducted will help to answer this question. Some patients in our study received colistin with fosfomycin. A randomized controlled study comparing colistin alone with colistin combined with fosfomycin for therapy of carbapenem-resistant *A. baumannii* infections at Siriraj Hospital found the eradication rate of causative bacteria from infection sites to be higher in the drug combination group with no mortality benefit[23]. Only a few patients in the present study received tigecycline. Although tigecycline

is usually active against most strains of carbapenem-resistant *A. baumannii* isolated from Thai patients[23], two previous clinical studies found no benefit in using tigecycline for therapy in carbapenem-resistant *A. baumannii* infections[24,25].

In summary, colistin remains the principal antibiotic for therapy in carbapenem-resistant Gram-negative bacterial infections in Thailand. Colistin's effectiveness and safety is still rated as moderate for therapy in difficult-to-treat resistant Gram-negative bacterial infections.

What is already known on this topic?

Colistin has moderate effectiveness and safety for therapy of severe infections caused by carbapenem-resistant Gram-negative bacteria.

What this study adds?

Colistin is still the backbone antibiotic for therapy of severe infections caused by carbapenem-resistant Gram-negative bacteria.

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Potential conflicts of interest

None.

References

1. Rongrungruang Y, Sawanpanyalert N, Chomdacha P, Surasarang K, Wiruchkul N, Kachintorn K, et al. Health-care associated infections in Thailand 2011. J Med Assoc Thai 2013; 96 (Suppl 2): S117-23.
2. Chung DR, Song JH, Kim SH, Thamlikitkul V, Huang SG, Wang H, et al. High prevalence of multidrug-resistant nonfermenters in hospital-acquired pneumonia in Asia. Am J Respir Crit Care Med 2011; 184: 1409-17.
3. Werarak P, Kiratisin P, Thamlikitkul V. Hospital-acquired pneumonia and ventilator-associated pneumonia in adults at Siriraj Hospital: etiology, clinical outcomes, and impact of antimicrobial resistance. J Med Assoc Thai 2010; 93 (Suppl 1): S126-38.
4. Werarak P, Waiwarawut J, Tharavichitkul P, Pothirat C, Rungruanghiranya S, Geater SL, et al. *Acinetobacter baumannii* nosocomial pneumonia in tertiary care hospitals in Thailand. J Med Assoc Thai 2012; 95 (Suppl 2): S23-33.
5. Bergen PJ, Landersdorfer CB, Lee HJ, Li J, Nation RL. 'Old' antibiotics for emerging multidrug-resistant bacteria. Curr Opin Infect Dis 2012; 25: 626-33.
6. Barnett M, BushbySR, Wilkinson S. Sodium sulphomethyl derivatives of polymyxins. Br J Pharmacol Chemother 1964; 23: 552-74.
7. Bergen PJ, Li J, Rayner CR, Nation RL. Colistin methanesulfonate is an inactive prodrug of colistin against *Pseudomonas aeruginosa*. Antimicrob Agents Chemother 2006; 50: 1953-8.
8. Koomanachai P, Tiengrim S, Kiratisin P, Thamlikitkul V. Efficacy and safety of colistin (colistimethate sodium) for therapy of infections caused by multidrug-resistant *Pseudomonas aeruginosa* and *Acinetobacter baumannii* in Siriraj Hospital, Bangkok, Thailand. Int J Infect Dis 2007; 11: 402-6.
9. Garonzik SM, Li J, Thamlikitkul V, Paterson DL, Shoham S, Jacob J, et al. Population pharmacokinetics of colistin methanesulfonate and formed colistin in critically ill patients from a multicenter study provide dosing suggestions for various categories of patients. Antimicrob Agents Chemother 2011; 55: 3284-94.
10. Bellomo R, Ronco C, Kellum JA, Mehta RL, Palevsky P. Acute renal failure - definition, outcome measures, animal models, fluid therapy and information technology needs: the Second International Consensus Conference of the Acute Dialysis Quality Initiative (ADQI) Group. Crit Care 2004; 8: R204-12.
11. Cheng CY, Sheng WH, Wang JT, Chen YC, Chang SC. Safety and efficacy of intravenous colistin (colistin methanesulphonate) for severe multidrug-resistant Gram-negative bacterial infections. Int J Antimicrob Agents 2010; 35: 297-300.
12. Kwon KH, Oh JY, Yoon YS, Jeong YJ, Kim KS, Shin SJ, et al. Colistin treatment in carbapenem-resistant *Acinetobacter baumannii* pneumonia patients: Incidence of nephrotoxicity and outcomes.

Int J Antimicrob Agents 2015; 45: 605-9.
13. Binh NG, Hayakawa K, Co DX, Tuan ND, Anh NH, Thuy NT, et al. The efficacy and nephrotoxicity associated with colistin use in an intensive care unit in Vietnam: use of colistin in a population of lower body weight. Int J Infect Dis 2015; 35: 18-23.
14. Khawcharoenporn T, Pruetpongpun N, Tiamsak P, Rutchanawech S, Mundy LM, Apisarnthanarak A. Colistin-based treatment for extensively drug-resistant *Acinetobacter baumannii* pneumonia. Int J Antimicrob Agents 2014; 43: 378-82.
15. Vandepitte WP, Berge J, Andersson R. Clinical outcomes of children with carbapenem-resistant *Acinetobacter baumannii* bacteremia. J Med Assoc Thai 2014; 97 (Suppl 11): S129-39.
16. Rattanaumpawan P, Lorsutthitham J, Ungprasert P, Angkasekwinai N, Thamlikitkul V. Randomized controlled trial of nebulized colistimethate sodium as adjunctive therapy of ventilator-associated pneumonia caused by Gram-negative bacteria. J Antimicrob Chemother 2010; 65: 2645-9.
17. Ni W, Shao X, Di X, Cui J, Wang R, Liu Y. In vitro synergy of polymyxins with other antibiotics for *Acinetobacter baumannii*: a systematic review and meta-analysis. Int J Antimicrob Agents 2015; 45: 8-18.
18. Durante-Mangoni E, Signoriello G, Andini R, Mattei A, De Cristoforo M, Murino P, et al. Colistin and rifampicin compared with colistin alone for the treatment of serious infections due to extensively drug-resistant *Acinetobacter baumannii*: a multicenter, randomized clinical trial. Clin Infect Dis 2013; 57: 349-58.
19. Garnacho-Montero J, Amaya-Villar R, Gutierrez-Pizarraya A, Espejo-Gutierrez dT, Artero-Gonzalez ML, Corcia-Palomo Y, et al. Clinical efficacy and safety of the combination of colistin plus vancomycin for the treatment of severe infections caused by carbapenem-resistant *Acinetobacter baumannii*. Chemotherapy 2013; 59: 225-31.
20. Batirel A, Balkan II, Karabay O, Agalar C, Akalin S, Alici O, et al. Comparison of colistin-carbapenem, colistin-sulbactam, and colistin plus other antibacterial agents for the treatment of extremely drug-resistant *Acinetobacter baumannii* bloodstream infections. Eur J Clin Microbiol Infect Dis 2014; 33: 1311-22.
21. López-Cortés LE, Cisneros JM, Fernández-Cuenca F, Bou G, Tomás M, Garnacho-Montero J, et al. Monotherapy versus combination therapy for sepsis due to multidrug-resistant *Acinetobacter baumannii*: analysis of a multicentre prospective cohort. J Antimicrob Chemother 2014; 69: 3119-26.
22. Falagas ME, Lourida P, Poulikakos P, Rafailidis PI, Tansarli GS. Antibiotic treatment of infections due to carbapenem-resistant Enterobacteriaceae: systematic evaluation of the available evidence. Antimicrob Agents Chemother 2014; 58: 654-63.
23. Sirijatuphat R, Thamlikitkul V. Preliminary study of colistin versus colistin plus fosfomycin for treatment of carbapenem-resistant *Acinetobacter baumannii* infections. Antimicrob Agents Chemother 2014; 58: 5598-601.
24. Tiengrim S, Tribuddharat C, Thamlikitkul V. In vitro activity of tigecycline against clinical isolates of multidrug-resistant *Acinetobacter baumannii* in Siriraj Hospital, Thailand. J Med Assoc Thai 2006; 89 (Suppl 5): S102-5.
25. Chuang YC, Cheng CY, Sheng WH, Sun HY, Wang JT, Chen YC, et al. Effectiveness of tigecycline-based versus colistin-based therapy for treatment of pneumonia caused by multidrug-resistant *Acinetobacter baumannii* in a critical setting: a matched cohort analysis. BMC Infect Dis 2014; 14: 102.
26. Cheng A, Chuang YC, Sun HY, Sheng WH, Yang CJ, Liao CH, et al. Excess mortality associated with colistin-tigecycline compared with colistin-carbapenem combination therapy for extensively drug-resistant *Acinetobacter baumannii* bacteremia: a multicenter prospective observational study. Crit Care Med 2015; 43: 1194-204.

การติดตามประสิทธิผลและความปลอดภัยของการใช้ยาโคลิสตินรักษาผู้ป่วยติดเชื้อแบคทีเรียกรัมลบที่ดื้อยาต้านจุลชีพที่โรงพยาบาลศิริราช

วิษณุ ธรรมลิขิตกุล, สุคนทิพย์ โพธิ์พุ่ม

วัตถุประสงค์: *เพื่อติดตามประสิทธิผลและความปลอดภัยของการใช้ยาโคลิสตินรักษาผู้ป่วยติดเชื้อแบคทีเรียกรัมลบดื้อยาต้านจุลชีพที่โรงพยาบาลศิริราช หลังจากมีการใช้ยานี้ในประเทศไทยเป็นครั้งแรกที่โรงพยาบาลศิริราชเมื่อ 10 ปีก่อน*

วัสดุและวิธีการ: *ศึกษาผู้ป่วยผู้ใหญ่ในโรงพยาบาลศิริราชที่มีการติดเชื้อแบคทีเรียกรัมลบดื้อยาต้านจุลชีพซึ่งได้รับยาฉีดโคลิสติน (Colistate®) ระหว่างเดือนตุลาคม พ.ศ. 2557 ถึง มิถุนายน พ.ศ. 2558 โดยนำข้อมูลจากเวชระเบียนผู้ป่วย ได้แก่ ลักษณะทั่วไป ลักษณะของการติดเชื้อ การรักษาด้วยยาต้านจุลชีพ ผลการรักษาทางคลินิก ผลการตอบสนองทางจุลชีววิทยา และพิษต่อไต มาวิเคราะห์ด้วยสถิติเชิงพรรณนา*

ผลการศึกษา: *ผู้ป่วยที่นำมาวิเคราะห์มีจำนวน 138 ราย ผู้ป่วยส่วนมากเป็นชายสูงอายุ การติดเชื้อที่พบบ่อยที่สุด คือ ปอดอักเสบติดเชื้อ เชื้อก่อโรคที่พบบ่อยที่สุด คือ A. baumannii เชื้อ A.baumannii และ P.aeruginosa แทบทุกสายพันธุ์ดื้อยากลุ่ม carbapenems ผู้ป่วยร้อยละ 94.9 ได้รับโคลิสตินครั้งแรกในขนาดสูง (300 มิลลิกรัม) ผู้ป่วยร้อยละ 19.6 ได้รับโคลิสตินขนานเดียว ผู้ป่วยส่วนมากได้รับยาต้านจุลชีพอื่นร่วมด้วยโดยเฉพาะอย่างยิ่งยากลุ่ม carbapenems และ piperacillin-tazobactam ผู้ป่วยร้อยละ 71.7 ตอบสนองต่อการรักษาเมื่อสิ้นสุดการรักษาด้วยโคลิสติน ผู้ป่วยร้อยละ 23.2 เสียชีวิตเมื่อสิ้นสุดการรักษาด้วยโคลิสติน และผู้ป่วยร้อยละ 39.9 เสียชีวิตในวันที่ 30 หลังการรักษาด้วยโคลิสติน ผู้ป่วยร้อยละ 50 กำจัดเชื้อให้หมดจากตำแหน่งที่มีการติดเชื้อเมื่อสิ้นสุดการรักษาด้วยโคลิสติน ผู้ป่วยร้อยละ 39.9 เกิดพิษต่อไตโดยพิษต่อไตส่วนมากไม่รุนแรงและการทำงานของไตมักกลับสู่ภาวะเดิมได้*

สรุป: *ยาโคลิสตินยังคงเป็นยาที่มีความสำคัญในการรักษาการติดเชื้อแบคทีเรียกรัมลบดื้อยากลุ่ม carbapenem ยาโคลิสตินยังมีประสิทธิผลและความปลอดภัยปานกลางในการรักษาการติดเชื้อแบคทีเรียกรัมลบดื้อยาที่รักษาได้ยาก*