

Efficacy and Safety of Colistin for Treatment of Multidrug-Resistant *Acinetobacter Baumannii*

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ABSTRACT

Background: Antibiotic resistance of *Acinetobacter baumannii* causes various communicable diseases and increases the risks of admission to intensive care units (ICUs) with high morbidity and mortality rates.

Objectives: Evaluating the efficacy of colistin usage guidelines and recommendations among critically ill patient infected by a multidrug-resistant *Acinetobacter baumannii*.

Methods: An observational cross sectional study that was performed during the period from June to August 2017 among 127 critically ill patients who were treated with colistin for multidrug-resistant *Acinetobacter baumannii* using bacterial culture and proper identification methods. Evaluations of CRP, bacterial culture, BUN and serum creatinine level were routinely done pre- and post-treatment.

Results: The method of administrating colistin was through intravenous infusion among all the patients and the most common indication of colistin usage were pneumonia followed by UTI. All the patients were susceptible to colistin and shown a negative bacterial cultures among most of the patients. The creatinine level was elevated (>2 mg/dL) showing nephrotoxicity among 11% of the patient. No allergic, neurological effects or mortality rates were observed in the study.

Conclusion: The findings of the recent study revealed that colistin is the best therapeutic treatment for *A. baumannii* in KSA hospitals due to their broad-spectrum activity that may make them the most important choice for serious communicable and hospital acquired infections. Proper monitoring of the side-effects of colistin especially nephrotoxic effects through routine evaluation of creatinine level to detect the renal injury and adjusting the doses or combination of colistin low dose with other antibiotics.

Keywords: Colistin, *Acinetobacter baumannii* (*A. baumannii*), resistance, monitoring, critically Ill, KSA.

INTRODUCTION

Bacterial resistance against antibiotics is a major health problem around the world that impacts the urgent need for development of new medications that may not be available and cost time and money^(1, 2). The resistance of gram negative bacteria outbreaks including *Pseudomonas species* and *Acinetobacter species* could result in vast worldwide health implications and increase morbidity and mortality rate⁽³⁾. *Acinetobacter baumannii*, (*A. baumannii*) is a gram positive opportunistic pathogen that causes various communicable diseases and increases the risks of admission to intensive care units (ICUs) with high morbidity and mortality rates⁽⁴⁻⁶⁾.

The treatment of choice for *Acinetobacter species* is carbapenems medication but due to the overuse of these medications has resulted in development of Metallo beta lactamase (MBL) producing bacteria⁽⁷⁾. Although, some antibiotics still active against this type of bacteria^(5, 8).

The Polymyxins are being used for many years for treatment of Metallo beta lactamase (MBL) producing bacteria as they consisted of 5 different compounds with polypeptide less toxic antibiotics

that chiefly works on the bacterial cytoplasmic membrane of bacterial cell^(4, 9).

Colistin is a polymyxin E that is clinically used for *Acinetobacter (A.) baumannii*^(10, 11). However, some adverse effects of colistin including renal, pulmonary and neurological toxicities after intravenous injection⁽¹²⁾. Furthermore, some patients may suffer from gastrointestinal events, allergic reactions and pulmonary toxicities⁽¹³⁾.

AIM OF STUDY

The present study aimed to evaluate the efficacy of colistin usage guidelines and recommendations among critically ill patients infected by a multidrug-resistant *Acinetobacter baumannii*.

METHODS

Study design:

An observational cross sectional study that was conducted at King Abdullah Hospital (KAH) - bishah, Kingdom of Saudi Arabia (KSA), from June to August 2017.

Study population:

All the patients who were treated with colistin for multidrug-resistant *Acinetobacter baumannii* using

bacterial culture and proper identification methods were enrolled in the present study. The study included 127 patients during the study period.

Data collection:

The data collection was performed in the hospital under the supervision of senior clinical pharmacists. The data of the included patients comprised of demographic variables as age and sex. The history of medications, diagnosis and types of infections were recorded. Also, laboratory investigation as microbiological culture, serum creatinine, blood urea nitrogen (BUN) and C-reactive protein [CRP] were analyzed before and during initiation of treatment.

Ethical considerations

Ethical approval was obtained from the committee and institutional review board in King Abdullah Hospital and the policy of hospital was respected.

RESULTS

- **Demographics and clinical picture:**

A total of eligible 127 patients were included in the study, the mean age of patients ranged from 44-67 years old with a mean of 53.2 years old. Most of the patients (61.4%) were males while 38.6% were females. The method of administering colistin was through intravenous infusion among all the patients. Also, the indications of colistin usage were pneumonia among most of the participants followed by UTI then sepsis and wound infection.

Table 1: Socio-Demographic Characteristics of Included Participants

Age (Year)		
Mean±SD (Min.-Max.)	53.2±9.7 (47-67)	
Gender	No.	Percentage (%)
Female	49	38.6%
Male	78	61.4%
Indications of colistin usage		
Pneumonia	65	51.2%
Urinary tract infection	38	30%
Sepsis	15	11.8%
Wound infection	9	7%
Methods of colistin administration		
Intravenous infusion	127	100%

- **Laboratory investigations and nephrotoxicity:**
All the patients were susceptible to colistin even alone or in combination with tigecycline or with vancomycin. Bacterial cultures were assessed pre- and post-treatment where most of the patients (122 patients, 96.1%) had negative microbiological cultures and eradication of pathogens after 5-8 days of treatments also after 3 days of treatment, 96 patients (75.6%) had negative. While 3.9% still had positive bacterial cultures after 8 days of treatments. The CRP level was an indicator for colistin effectiveness where most of the patients showed reduced levels of CRP after treatment which decreased more with time. The serum BUN level showed no change either pre- or post-treatment while the creatinine level was elevated (>2 mg/dL) showing nephrotoxicity among 14 (11%) patients where the dose was adjusted among most of them.
- **Other side effects:**
The side effects of colistin even allergic or neurological were not observed among all the included patients including paresthesia, vertigo, apnea and muscle weakness.
- **Mortality rates:**
None of the patients died during the treatment period and the doses of colistin were adjusted after showing nephrotoxicity.

DISCUSSION

Antibiotic resistance has emerged during the last decades due to low awareness and practice pattern of appropriate and correct or excessive usage of antibiotics^(14,15). In the present study, the indications of using colistin were pneumonia in most of the cases followed by urinary tract infections, sepsis and the least was wound infection. In the same respect, using colistin for treatment of hospital acquired infections especially pneumonia and UTI^(10,16,17).

This study showed that all of the isolates were susceptible to colistin after treatment and most of the patients (122 patients, 96.1%) had negative microbiological cultures and eradication of pathogens after 5-8 days of treatments also after 3 days of treatment, 96 patients (75.6%) had negative. While 3.9% still had positive bacterial cultures after 8 days of treatments. Consistent studies showed that most of isolated *A. baumannii* were susceptible to colistin^(18,19). Also, lower rates resistance were found toward colistin among patients with??? at Shiraz hospital⁽¹⁴⁾. In addition, the same results were shown among most of the patients who were susceptible to colistin treatment either alone or with other antibiotics⁽²⁰⁻²²⁾.

The nephrotoxicity was present among 14 patients who had higher levels of creatinine thus the doses of colistin were adjusted till the values returned to normal which showed proper monitoring of the side effects of colistin among the patients^(23, 24). On the other hand, no allergic or neurotoxic effects were shown among the patients and this could be attributed to that most of the patients administrated sedatives and analgesics.

Also, the levels of serum creatinine evaluated routinely during colistin treatment. In contrast, renal injury was found to be the most common adverse effect of colistin treatment and this could be attributed to improper patients monitoring during the treatment period^(16,25).

CONCLUSION

The findings of the recent study revealed that colistin is the best therapeutic treatments for *A.baumannii* in KSA hospitals due to their broad-spectrum activity that may make them the most important choice for serious communicable and hospital acquired infections. Proper monitoring of the side-effects of colistin especially nephrotoxic effects through routine evaluation of creatinine level to detect the renal injury and adjusting the doses or combination of colistin with other antibiotics.

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