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شبكة المعلومات الجامعية

التوثيق الالكتروني والميكروفيلم

شبكة المعلومات الجامعية

جامعة عين شمس

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قسم

نقسم باللّه العظيم أن المادة التي تم توثيقها وتسجيلها علي هذه الأقراص المدمجة قد أعدت دون أية تغيرات

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تحفظ هذه الأقراص المدمجة بعيدا عن الغبار

Efficacy of Nebulized Colistin-Based Monotherapy versus Intravenous Administration of Colistin in Treatment of Ventilator Associated Pneumonia Caused by Multidrug Resistant Gram-Negative Bacteria

Thesis

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List of Abbreviations

Abb.	Full term
AKI	*Acute kidney injury*
APACHE	*Acute physiology and chronic health evaluation*
BAL	*Bronchoalveolar lavage*
CDC	*Centers for Disease Control and Prevention*
CF	*Cystic fibrosis*
CMS	*Colistin methanesulfonate*
CPIS	*Clinical Pulmonary Infection Score*
CTs	*Computed tomograms*
ECDC	*European Centre for Disease Prevention and Control*
ELF	*Epithelial lining fluid*
GNB	*Gram-negative bacteria*
HAP	*Hospital acquired pneumonia*
HCAP	*Healthcare-associated pneumonia*
HS	*Highly significant*
ICU	*Intensive care unit*
IV	*Intravenous*
LOS	*Length of hospital stay*
LPS	*lipopolysaccharide*
MDR	*Multidrug-resistant*
MDRO	*Multidrug resistant organism*
MRSA	*Methicillin resistant S. aureus*
MV	*Mechanical ventilation*
NS	*Non significant*
S	*Significant*
VAP	*Ventilator-associated pneumonia*
XDR	*Extensively drug-resistant*

INTRODUCTION

Ventilator-associated pneumonia (VAP) is a grave cause of morbidity and mortality, complicating approximately 10 to 25% of all ICU patients, with an estimated mortality between 24 and 76%, which is 6–21 times higher in the intubated patients. Also VAP is one of the most common intensive care unit (ICU)-acquired infections that are associated with a prolonged duration of antibacterial treatment, length of hospital stay (LOS), and mechanical ventilation (MV), as well as high mortality and healthcare costs ***(Dasgupta et al., 2015).***

Increasing number of infection cases caused by multidrug resistant organism (MDRO) has become a significant problem worldwide due to the continuous rising of resistance to many classes of antibiotics. Mutant isolates such as fluoroquinolone-resistant and -lactamase-resistant bacteria have been frequently encountered, particularly in intensive care unit (ICU). During the last two decades, there have been less studies of developing antibiotics in search of discovering new type of antibiotics; meanwhile, the resistance of Gram-negative bacteria or MDRO to antibiotics is increasing ***(Orsi et al., 2011).***

Patients with ventilator-associated pneumonia (VAP) caused by multidrug resistant Gram-negative bacteria may be predisposed to poor outcome because of limited therapeutic options and the likelihood of ineffective empirical antibiotic therapy ***(Tseng et al., 2012).***

Colistin or polymyxin E is an old antibiotic, which has been used since 1959 for treating infection caused by Gram-negative MDRO. But because of its serious side effects as nephrotoxicity and neurotoxicity; therefore, the use of this antibiotic was stopped and it was replaced by other antibiotics which were effective and were considered safer at that time. However, the emergence of bacteria resistant to most classes of commercially available antibiotics and the shortage of new antimicrobial agents with activity against gram-negative microorganisms have led to the reconsideration of polymyxins as a valuable therapeutic option ***(Loho and Dharmayanti, 2015).***

The target of antimicrobial activity of colistin is the bacterial cell membrane. Electrostatic interactions between the cationic polypeptide (colistin) and anionic lipopolysaccharide (LPS) molecules in the outer membrane of the gram-negative bacteria, which leads to derangement of the cell membrane. Colistin displaces magnesium (Mg^{+2}) and calcium (Ca^{+2}), (which normally stabilize the LPS molecules), from the negatively charged LPS, leading to a local disturbance of the outer membrane. The result of this process causes an increase in the permeability of the cell envelope, leakage of cell contents and cell death.

Recent studies revealed that nebulized colistin-based therapy, even without concurrent administration of intravenous colistin, may be an effective and safe treatment option for VAP caused by carbapenem-resistant *MDR-GNB* ***(Kim et al., 2017).***

The use of nebulized colistin in critically ill patients is effectively achieved in high concentrations in the lungs, without much systemic involvement. This study is important because of acute kidney injury (AKI) during intravenous colistin therapy remains a great concern, particularly in elderly patients in intensive care units (ICU) with impaired renal function and concomitant use of other nephrotoxic agents ***(Balkan et al., 2014; Athanassa et al., 2012).***

AIM OF THE WORK

The aim of study is to analyze the efficacy of nebulized colistin-based monotherapy versus intravenous administration of colistin in microbiological eradication and clinical improvement of patients with Ventilator Associated Pneumonia caused by multidrug resistant Gram-negative bacteria.