Efficacy of nebulized colistin versus nebulized amikacin plus ceftazidime in treatment of ventilator associated pneumonia caused by Gram negative multidrug resistant organisms.

M.Sc. Thesis

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List of abbreviations

Abbreviation	Title
ARDS	Adult Respiratory Distress Syndrome
AUC	Area Under Curve
CAP	Community Acquired Pneumonia
CMS	Colistimethate Sodium
CPIS	Clinical Pulmonary Infection Score
CRP	C-Reactive Protein
CT	Computed Tomography
CXR	Chest X Ray
ESBL	Extended Spectrum Beta Lactamase
ETT	Endotracheal Tube
GER	Gastro Esophageal Reflux
GNB	Gram Negative Bacteria
HMEs	Heat and Moist Exchange humidifiers
HVLP	High Volume Low Pressure
ICU	Intensive Care Unit
IU	International Unit
L-Dab	L- diaminobutyric acid
LPS	Lipopolysaccharide
MDR	Multi Drug Resistant

mg	Milligrams
MIC	Minimal Inhibitory Concentration
MV	Mechanical Ventilation
r RNA	Ribosomal Ribonucleic Acid
t RNA	Transfer Ribonucleic Acid
TLC	Total Leucocyte Count
TNF- α	Tumor Necrosis Factor – α
VAP	Ventilator Associated Pneumonia

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1. Introduction

Ventilator-associated pneumonia (VAP) complicates the course of 8 to 28% of patients on mechanical ventilator (MV). Mortality rate for VAP ranges from 24 to 50% and may reach 76% in specific situation or when lung infection is caused by high risk pathogens. **(Chastre J and Fagon JY., 2002).**

The main pathogenic factor in VAP is the biofilm formed within the endotracheal tube (ETT). The oropharynx becomes colonized by aerobic gram negative bacteria after critical illness, antibiotic administration, hospital admission, and pooling of secretions above the ETT cuff causing VAP. The ETT prevents effective coughing so micro-aspiration of secretions occurs. The longer the duration of ventilation; the greater the risk of developing VAP. Nursing patients in supine position increases the risk of micro-aspiration and VAP development. **(P Gunasekera and A Gratrix., 2016**).

Significant proportion of patients in intensive care unit (ICU) receive antibiotics that may not be indicated, and furthermore, if antibiotics are not discontinued in light of negative cultures, a full course of unnecessary antibiotics

may be administered, which facilitate emergence of Multi Drug Resistant (MDR) organisms, which worsen the patient outcome. **(McGowan JJE., 2006).**

Of the MDR organisms, highly resistant Gram-negative bacteria (GNB) (e.g. MDR carbapenemase-producing *Klebsiella pneumonia* and *Acinetobacter spp*.) require special mention; these organisms can be resistant to all currently available antimicrobial agents or remain susceptible only to older, potentially more toxic agents such as the polymyxins, leaving limited and sub-optimal options for treatment. **(Bonomo RA and Szabo D., 2006).**

Administration of antimicrobials through aerosol allows for the depositions of antimicrobial agents directly at the site of infection, in concentrations higher than systemic administration. The adjunctive use of nebulized antimicrobial agents has been widely used in the treatment of patients with cystic fibrosis and has gained much interest in treatment of VAP, especially with the rapid emergence of MDR organisms in many ICUs. Nebulized antibiotics such as colisin have been used to successfully treat infections caused by a variety of MDR organisms such as P.aeroginosa or Acinetobacter species, resistant to most or

all available antimicrobial drugs that can be administered systemically. **(Palmer L B., 2009).**

Relapse and recurrence after initial treatment are also common, and mono-therapy with nebulized antibiotics could be an alternative treatment as it is difficult to achieve microbiological eradication for certain pathogens, including MDR organisms in VAP**. (Rangel EL et al., 2009).**

2- Aim of the work

Aim of this study is to compare efficacy of nebulized colistin versus nebulized amikacin and ceftazidime in treatment of ventilator associated pneumonia caused by Gram negative organisms.