UNIVERSITI TEKNOLOGI MARA

AN OUTCOME STUDY OF EXTENDED VERSUS STANDARD INFUSION OF MEROPENEM IN SEPTIC CRITICALLY ILL PATIENTS

FAHMI BIN HASSAN

Thesis submitted in fulfillment of the requirements for the degree of **Master of Science**

Faculty of Pharmacy

April 2016

CONFIRMATION BY PANEL OF EXAMINERS

I certify that a Panel of Examiners has met on 27th April 2015 to conduct the final examination of Fahmi Bin Hassan on his Master of Science thesis entitled "An Outcome Study of Extended versus Standard Infusion of Meropenem in Septic Critically Ill Patients" in accordance with Universiti Teknologi MARA Act 1976 (Akta 173). The Panel of Examiners recommends that the student be awarded the relevant degree. The panel of Examiners was as follows:

Jean-Frederic Faizal Weber, PhD Professor Faculty of Pharmacy Universiti Teknologi Mara (Chairman)

Mohamed Mansor Bin Manan, PhD Professor Faculty of Pharmacy Universiti Teknologi Mara (Internal Examiner)

Mohamed Baidi Bin Bahari, PhD Professor Faculty of Pharmacy AIMST University (External Examiner)

SITI HALIJJAH SHARIFF, PhD

Associate Professor Dean Institute of Graduates Studies Universiti Teknologi MARA Date: 12th April 2016 **AUTHOR'S DECLARATION**

I declare that the work in this thesis/dissertation was carried out in accordance with

the regulations of Universiti Teknologi MARA. It is original and is the results of my

own work, unless otherwise indicated or acknowledged as referenced work. This

thesis has not been submitted to any other academic institution or non-academic

institution for any degree or qualification.

I, hereby, acknowledge that I have been supplied with the Academic Rules and

Regulations for Post Graduate, Universiti Teknologi MARA, regulating the conduct

of my study and research.

Name of Student : Fahmi Bin Hassan

Student I.D. No. : 2010324999

Program : Master of Science (Clinical Pharmacy) – PH780

Faculty : Pharmacy

Thesis Tittle : An Outcome Study of Extended versus Standard

Infusion of Meropenelm in Septic Critically III Patients

Signature of Student:

Date : April 2016

iii

ABSTRACT

Sepsis incidence in critical care settings is a major problem in health care. Good choice of antibiotic treatment may improve the outcome of patients with sepsis. Meropenem is one of the most widely used antibiotics for treatment of serious bacterial infection in hospitalized patients. Since meropenem is a beta-lactam antibiotic, it exhibits the bactericidal effect with time-dependent activity. Currently ICUs in Malaysia do not have a standard guideline on how to infuse meropenem; whether to use 30-minute or three-hour infusion due to the lack of clinical evidence supporting either methods. The objective of this study is to compare the clinical outcomes of critically ill patients with sepsis receiving 30-minute meropenem infusion and three-hour meropenem infusion. A retrospective case control study was conducted among patients over 18 years old who were diagnosed with sepsis and treated with meropenem infusion in Intensive Care Unit of three hospitals in Malaysia. Patients included in the study received either 30-minute infusion of meropenem or three-hour infusion of meropenem as per practice of individual settings. Outcomes and clinical data were retrospectively collected from the electronic databases and also patients file from the record departments of individual settings. During the study period, a total of 1975 patients received meropenem infusion during their admission in the ICUs of the three selected hospitals. 11.4% of the selected samples met the inclusion criteria of the study and were included in the analysis. From the 225 subjects, 108 patients received three-hour infusion of meropenem while the remaining 117 patients received 30-minute infusion of meropenem. Patients receiving the extended infusion of meropenem were found to have significantly lower mortality rate, shorter length of hospital stay, and higher rate of fever and white blood cell reduction. This study would be able to strengthen the evidence in using prolonged infusion of meropenem as a standard practice in critical care settings in Malaysia. As this is the first study of its kind done in Malaysia, it proves that prolonged meropenem infusion may be beneficial to critically ill patients with sepsis. However, a randomized clinical trial with large sample size should be carried out in local settings in order to improve the result of the study and minimizes other confounders that may influence with the result of the study.

TABLE OF CONTENTS

	Page
CONFIRMATION BY PANEL OF EXAMINERS	ii
AUTHOR'S DECLARATION	iii
ABSTRACT	iv
ACKNOWLEGEMENT	v
TABLE OF CONTENTS	vi
LIST OF TABLES	X
LIST OF FIGURES	xii
CHAPTER ONE: INTRODUCTION	14
1.1 Defining Sepsis	14
1.2 Sepsis Sources and Responsible Pathogens	17
1.3 Impact of Sepsis	17
1.4 Prognosis of ICU Patients with Sepsis	18
1.5 Sepsis and Organ Failure	18
1.6 The Role of Disease Severity Scoring System	19
1.6.1 APACHE II and SAPS II Scoring System	20
1.7 Gram Negative Infection in Sepsis	23
1.8 Antimicrobial Treatment in Sepsis	25
1.9 Problem Statement	28
1.9.1 Research Question	30
1.9.2 Research Hypothesis	30
1.9.3 Purpose of the Study	30
1.10 Significance of Study	31
CHAPTER TWO: LITERATURE REVIEW	32
2.1 Introduction	32
2.2 Overview of Meropenem	32
2.3 Meropenem Stability	36