

EFFECT OF EMPIRICAL FLUCONAZOLE IN TREATMENT OF SEPSIS

An Essay

Submitted in Partial Fulfillment for Master Degree
in Intensive Care

By

Mina George Danial

*M.B.,B.Ch,
Faculty of Medicine – Cairo University*

Supervisors

Prof.Dr.Bassem Boulos Ghobrial

*Professor of Anesthesiology and Intensive Care
Faculty of Medicine - Ain Shams University*

Assist. Prof. Dr. Karim Youssef Kamal Hakim

*Assistant Professor of Anesthesiology and Intensive Care
Faculty of Medicine - Ain Shams University*

Dr.SanaaFarag Mahmoud

*Lecturer of Anesthesiology and Intensive Care
Faculty of Medicine - Ain Shams University*

**Faculty of Medicine
Ain Shams University**

2014

تأثير اعطاء عقار الفلوكونازول فى علاج التسمم البكتيرى

رسالة مقدمة من

الطبيب/مينا جورج دانيال
بكالوريوس الطب والجراحة
جامعة القاهرة

توطنه للحصول على درجة ماجستير
فى العناية المركزة

تحت اشراف

الاستاذ الدكتور/باسم بولس غبريال
استاذ التخدير والعناية المركزة
كلية الطب - جامعة عين شمس

الدكتور/كريم يوسف كمال حكيم
استاذ مساعد التخدير والعناية المركزة
كلية الطب - جامعة عين شمس

الدكتورة/سناء فرج محمود
مدرس التخدير والعناية المركزة
كلية الطب - جامعة عين شمس

كلية الطب
جامعة عين شمس
2014

CONTENTS

1- Introduction	1
2- Aim of the Work.....	3
3- Pathophysiology of Sepsis.....	4
4- Management of Sepsis.....	29
5- Fluconazole and Sepsis.....	53
6- Summary.	84
7- References.	86
8- Arabic Summary.....	--



Acknowledgement

*I would like to express my sincere gratitude to **Prof. Dr. Bassem Boulos Ghobrial**, Professor of Anesthesiology and Intensive Care, Faculty of Medicine - Ain Shams University, firstly for giving me the honor to be his student and for his great support and stimulating views.*

*Also I would like to extend my warmest gratitude to **Assist. Prof. Dr. Karim Youssef Kamal Hakim**, Assistant Professor of Anesthesiology and Intensive Care, Faculty of Medicine - Ain Shams University, his hard and faithful efforts have helped me to do this work.*

*I would like to thank **Dr. Sanaa Farag Mahmoud**, Lecturer of Anesthesiology and Intensive Care, Faculty of Medicine - Ain Shams University, her active, persistent guidance and other whelming kindness have been of great help through this work.*

*Also I would like to thank my **Family** who stood behind me to finish this work and for their great support.*

✍ Mina George Danial



Introduction



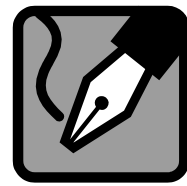
Aim of the Work



Pathophysiology of Sepsis



Management of Sepsis



Fluconazole and Sepsis



Summary



References



Arabic Summary

INTRODUCTION

Sepsis is defined by consensus conference as "the systemic inflammatory response syndrome that occurs during infection" it is generally viewed as a disease aggravated by the inappropriate immune response encountered in the affected individual (*Almoget al., 2004*).

In sepsis, the inflammatory response is an attempt by the body toward off pathogens but it is often uncontrolled and detrimental, which may lead to irreversible functional and structural damage to various organ systems of the host. It is generally accepted that tissue damage in inflammatory conditions is caused primarily by host effector cells, rather than by the initiating agent (*Carey et al., 1992*). The greater the degree of organ dysfunction produced by septic shock, the greater the resultant mortality (*Marshall et al., 1995*).

Fluconazole (FLZ) is a well-tolerated antifungal drug with a demonstrated ability to reversibly penetrate into human PMNs. Unlike ketoconazole, which is available only as an oral preparation, fluconazole can be administered intravenously. Fluconazole has been shown to improve survival and reduce multi-organ damage in experimental (*Tariq et al., 2003*) and clinical septic shock (*Jacobs et al., 2003*).

Since fluconazole has no inherent antibacterial properties, its beneficial effects in bacteremia have been attributed to its action on

the modulation of neutrophils sequestration and activation (*Zervos et al., 1996*).

Fluconazole has been suggested to increase the bactericidal activity of neutrophils, mostly through a non-cytokine-mediated pathway (*Forman and Torres, 2002*).

This study is therefore conducted to demonstrate the impact of fluconazole administration in patients with sepsis on their outcome and to determine whether this presumed protective effect may reduce the progression to multi-organ failure and mortality in these patients.

AIM OF THE WORK

Analysis the role of fluconazole in sepsis and septic shock.