



شبكة المعلومات الجامعية
التوثيق الإلكتروني والميكروفيلم

بسم الله الرحمن الرحيم



MONA MAGHRABY



شبكة المعلومات الجامعية
التوثيق الإلكتروني والميكروفيلم



شبكة المعلومات الجامعية التوثيق الإلكتروني والميكروفيلم



MONA MAGHRABY



شبكة المعلومات الجامعية
التوثيق الإلكتروني والميكروفيلم

جامعة عين شمس

التوثيق الإلكتروني والميكروفيلم

قسم

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



يجب أن

تحفظ هذه الأقراص المدمجة بعيدا عن الغبار



MONA MAGHRABY

Stress ulcer prophylaxis in the critically ill patients

A Systematic Review/Meta-Analysis

For partial fulfillment of Master Degree
In intensive Care

By

Emil Noshy Aziz Salh

M.B.B.Ch.

Under Supervision of

Prof. Dr. Ahmed Saeed Mohamed Ibrahim

Professor of Anesthesia and Intensive Care and Pain Management
Faculty of Medicine – Ain-Shams University

Prof. Dr. Sameh Salem Hefni Taha

Assistant Professor of Anesthesia and Intensive Care and Pain Management
Faculty of Medicine – Ain-Shams University

Dr. Samuel Habachi Daniel

Lecturer in Anesthesia and Intensive Care and Pain Management
Faculty of Medicine – Ain-Shams University

**Faculty of Medicine
Ain-Shams University
2020**



Acknowledgments

First and forever, thanks to **Allah**, Almighty for giving me the strength and faith to complete my thesis and for everything else.

Then I would like to express my sincere appreciation and gratitude to **Prof. Dr. Ahmed Saeed Mohamed Ibrahim**, Professor of Anesthesia and Intensive Care and Pain Management, Faculty of Medicine – Ain-Shams University, for his great support all through the whole work, for valuable guidance, and follow up of the progress of this work, I have been greatly honored by his supervision.

Profound and ultimate gratitude are expressed to **Prof. Dr. Sameh Salem Hefni Taha**, Assistant Professor of Anesthesia and Intensive Care and Pain Management, Faculty of Medicine – Ain-Shams University, for his continuous help in following up the progress of the work, his continuous support and encouragement were really invaluable.

Last but not least, I can't forget to thank **Dr. Samuel Habachi Daniel**, Lecturer in Anesthesia and Intensive Care and Pain Management, Faculty of Medicine – Ain-Shams University, for the efforts and time he has devoted to accomplish this work.

I would like to thank my **Parents** who sacrificed a lot for me for their continuous support, endless help and encouragement.

 **Emil Noshy Aziz Salh**



List of Contents

<i>Subject</i>	<i>Page No.</i>
List of Abbreviations.....	i
List of Tables	iv
List of Figures	v
Introduction	1
Aim of the Work.....	4
Review of Literature	
Definition, Epidemiology, Prevalence	5
Risk factors of Stress Ulceration.....	12
Pathogenesis of SRMD	17
Prophylaxis, Treatment and Prognosis	25
Materials and Method.....	49
Results.....	54
Discussion	69
Conclusion.....	79
Summary	80
References	82
Arabic Summary	—

List of Abbreviations

<i>Abbrev.</i>	<i>Full term</i>
ALB	Albumin
ALD	Alcoholic Liver Disease
ALF	Acute Liver Failure
ALT	Alanine transaminase
ASA	Acetylsalicylic acid
APACHE	Acute Physiology and Chronic Health Evaluation
APTT	A partial thromboplastin time
ARDS	The acute respiratory distress syndrome
ASHP	The American Society of Health-System Pharmacists
AST	Acid suppressive therapy
BSA	Body surface area
CAP	Community-acquired pneumonia
CA-UTI	Catheter –associated urinary tract infection
CDAD	Clostridium difficile–associated diarrhea
CENTRAL	Cochrane Central Register of Controlled Trials
CGRP	Calcitonin gene-related peptide
CI	Confidence interval
CLABSI	Central line –associated blood stream infection
CMM	Cancer specific Mortality Model
CRF	Corticotropin-releasing factor
CRI	Constant rate infusion
CYP450	Cytochrome P450
DVT	Deep venous thrombosis
EGD	Esophagogastroduodenoscopy
EGF	Epidermal growth factor
ELIZA	Enzyme-linked immunosorbant assay
EN	Enteral nutrition
GCS	Glasgow Coma Scale

GIT	Gastrointestinal tract
GMDS	Gastric mucosal defense system
GUD	Gastric ulcer disease
H pylori	Helicobacter pylori
H2-RAs	Histamine H2-receptor antagonist
HAIs	Health care –associated infections
ICH	Intracerebral Hemorrhage
I V	Intravenous administration
ICU	Intensive care unit
INR	International normalized ratio
LD	Loading dose;
LDH	Lactate dehydrogenase
LODS	The Logistic Organ Dysfunction System
MOOSE	Meta-analysis Of Observational Studies in Epidemiology
NG	Nasogastric tube
NSAIDs	Non-steroidal anti-inflammatory drugs
OGD	Oesophago-gastroduodenoscopy
OR	Odds ratio
PE	Pulmonary embolism
PG	Prostaglandin
PPIs	Proton pump inhibitors
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
PUD	Peptic ulcer disease
RCT	Randomized controlled trial
ROS	Reactive oxygen species
RR	Relative risk
SAH	Subarachnoid hemorrhage
SIRS	Systemic inflammatory response syndrome
SGOT	Serum glutamic oxaloacetic transaminase
SGPT	Serum glutamic pyruvate transaminase

List of Abbreviations

SIADH	Syndrome of inappropriate secretion of antidiuretic hormone
SMD.....	Standard mean deviated
SRI.....	Stress related Injury
SRMD	Stress related mucosal disease
SSI.....	Surgical site infection
SUCRA	Surface under the cumulative ranking curve
SUP	Stress ulcer prophylaxis
TFF	Trefoil factor family
TSA.....	Trial sequential analysis
UGIB	Upper gastrointestinal bleeding
VacA.....	Vacuolating cytotoxin A
VAP	Ventilator- associated pneumonia
VTE	Venous thromboembolism

List of Tables

<i>Table No.</i>	<i>Title</i>	<i>Page No.</i>
Table (1):	Stress ulcer in Critically Ill Patients	8
Table (2):	Risk factors of stress related mucosal disease in critically ill patients.....	12
Table (3):	The recommendation for SUP in critically ill patients.....	26
Table (4):	Drug to drug interactions with cimetidine	30
Table (5):	Drug to drug interactions with omeprazole	33
Table (6):	Comparison of the prophylactic safety and efficacy of H 2RAs and PPIs in ICU	37
Table (7):	Drug to drug interactions with sucralfate	39
Table (8):	Cause of UGIB	45
Table (9):	Indicators of high risk of Rebleeding or Mortalities in Patients with Non-variceal UGIB	48
Table (10):	Summary Characteristics of the included studies.....	55

List of Figures

<i>Figure No.</i>	<i>Title</i>	<i>Page No.</i>
Figure (1):	Mechanism of mucosal tissue damage.....	9
Figure (2):	Photographs by endoscopic of mucosal tissue damage:	10
Figure (3):	Gastric mucosal defense system.(GMDS).....	18
Figure (4):	Ulcer with visible vessel	47
Figure (5):	Ulcer with visible vessel after hemoclip placement.....	47
Figure (6):	PRISMA flow-chart.....	54
Figure (7):	Forest Plot of rates of clinically important GI bleeding	58
Figure (8):	Forest Plot of rates of overt GI bleeding	59
Figure (9):	Forest Plot of rates of mortality.....	60
Figure (10):	Forest Plot of rates of Pneumonia	61
Figure (11):	Forest Plot of rates of clinically important GI bleeding	62
Figure (12):	Forest Plot of rates of overt GI bleeding	64
Figure (13):	Forest Plot of rates of mortality.....	65
Figure (14):	Forest Plot of rates of clinically important GI bleeding	66
Figure (15):	Forest Plot of rates of mortality.....	68

Introduction

Stress Ulceration was an important cause of morbidity and mortality in critically ill patients. Early active treatment reduces the risk of clinically significant bleeding, stress ulcer prophylaxis therefore became a standard of care in all critically ill patients (*Paul, 2010*).

Multiple Stress-related mucosal disease (SRMD) is still associated with substantial mortality and costs, and prophylactic approaches, including enteral nutrition, are needed (*Alhazzani et al., 2017*).

In critically ill people SRMD is a common complication. The human literature has defined the term SRMD to encompass the continuum of stress-related injury (SRI) to stress ulcerations (SU) (*Spirt, 2004*).

Overt bleeding characterized by hematemesis, gross blood, or coffee ground material in nasogastric (NG) tube aspirates, melena, or hematochezia has a recorded frequency of 0.6–6% in critically ill patients not treated with gastroprotectant (*Andrea et al., 2011*).

High risk of stress-related GI bleeding in people includes respiratory failure requiring mechanical ventilation >48 h, coagulopathy, sepsis, acute kidney injury, hepatic dysfunction,

shock, trauma, burns > 35% of the body, neurologic trauma, surgery, myocardial infarction, multiple organ failure, aspiration pneumonia, organ transplant, major surgery, postsurgical states, prolonged ICU admission, ileus, and high-dose corticosteroid use (*Frandah et al., 2014*).

Stress ulcer prophylaxis (SUP) has been found to be efficient and thus considered as a standard of care in the intensive care unit (ICU), included in the mnemonic FASTHUG (Feeding, Analgesia, Sedation, Thromboembolic prophylaxis, Head of bed elevation, stress Ulcer prophylaxis, Glucose control) that was developed by ICU physicians to ensure that key aspects of care are addressed during each patient encounter (*Masson et al., 2013*).

The benchmark for SUP to prevent bleeding stress ulcer is based on the understanding of the pathophysiology and recognized risk factors. The incidence of GI bleeding in critically ill patients was reduced by 59% in patients treated with stress ulcer prophylaxis agents, in comparison with those treated with placebo or no prophylaxis (*Krag et al., 2014*).

Actual trends in SRMD prophylaxis is the use of sucralfate, PPIs or H2RAs. The proportion of critically ill patients receiving SUP is greater than 90% and although majority of them receive H2RAs (63.9%), PPIs (23%), and sucralfate (12.2%) (*Daley et al., 2013*).

Treatment strategies need to be evaluated on an individual basis, taking into account the expected benefits of therapy balanced against the patient's risk factors for GI bleeding and the risk of hospital acquired pneumonia or Clostridium difficile associated diarrhea (CDAD) in the local epidemiological context (*Bulger et al., 2013*).

Aim of the Work

The overall aims of the Stress ulcer prophylaxis in the critically ill patients is to determine the benefits and risks of stress ulcer prophylaxis SUP in ICU.