ROLE of NEUTROPHIL GELATINASE ASSOCIATED LIPOCALIN as an EARLY BIOMARKER of ACUTE KIDNEY INJURY in CRITICALLY ill PATIENTS

Essay

Submitted for partial fulfillment of Master Degree
In Intensive Care

By

Ahmed Elsayed Basyuoni Ahmed
M.B., B.Ch,

Under Supervision Of

Prof. Dr. Seif El-Islam Abd-Elaziz Shaheen

Professor of Anesthesia and Intensive care
Faculty of Medicine –Ain Shams University

Dr. Ahmed Mohammed El-Sayed El-Hennawy

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

Dr.Abd-Alaziz Abd-Allah Abd-Alaziz

Lecturer of Anesthesia and Intensive Care
Faculty of Medicine –Ain Shams University

Faculty of medicine
Ain shams university
2014


بسم الله الرحمن الرحيم
إقرأ باسم ربك الذي
خلق ﴿١﴾ خلق الإنسان
من علق ﴿٢﴾ إقرأ وربك
الاكرم ﴿٣﴾ الذي علم
بالقلم ﴿٤﴾ علم الإنسان
ما لم يعلم ﴿٥﴾
صدق الله العظيم
سورة العلق
(الآيات (١-٥)

First of all, I am deeply grateful to *ALLAH*

I would like to express my deepest gratitude and appreciation to **Prof. Dr. Seif El-Islam Abd-ElAziz Shaheen,** Professor of Anesthesiology and Intensive Care, Faculty of Medicine, Ain shams University, for his kind guidance, continuous help and support through this work and it was a great honor to finish this work under his supervision.

I am very grateful to **Dr. Ahmed Mohammed El-Sayed El-Hennawy,** Assistant Professor of Anesthesiology and Intensive Care, Faculty of Medicine, Ain Shams University for his positive supervision during the preparation of this essay and for the extensive time and effort to offer every possible help to complete this work.

Special appreciation to **Dr. Abd-Alaziz Abd-Allah Abd-Alaziz,** Lecturer of Anesthesiology and Intensive Care, Faculty of Medicine, Ain Shams University for his kind advice, valuable instructions and continuous support which was the corner stone in the completion of this work.

Last but not least, I would like to present a lot of thanks to my *father*, *mother* and my *wife*, whose without their help and support, this work could not come to birth.

Ahmed Elsayed

List of Contents

List of Abbreviations

ACEIs	Angiotensin converting enzyme inhibitors
ADH	Antidiuretic Hormone
ADQI	Acute Dialysis Quality Initiative
AKI	Acute kidney injury
AKIN	Acute Kidney Injury Network
ANCA	Anti neutrophil cytoplasmic antibody
ANP	Atrial Natruretic Peptide
ARF	Acute renal failure
ATN	Acute Tubular Necrosis
BUN	Blood Urea Nitrogen
CAVH	Continuous arteriovenous hemofiltration
CHD	Continuous hemodialysis
CHDF	Continuous hemodiafiltration
CHF	Continuous hemofiltration
CKD	Chronic kidney disease
CRRT	Continuous renal replacement therapy
CT	Computed tomography
CVC	Central venous catheter
CVP	Central venous pressure
CVVHDF	Continuous venovenous hemodiafiltration
DIC	Disseminated Intravascular Coagulopathy

List of Abbreviations (Cont...)

ELISA.....	Enzyme-linked immunosorbent assay
FENa	Fractional excretion of Na
GBM	Glomerular basement membrane
GFR	Glomerular filtration rate
Gro-α	Growth-related oncogene-α
HD	Hemodialysis
HIT	Heparin-induced thrombocytopenia
HUS	Hemolytic Uremic Syndrome
ICU	Intensive care unit
IHD	Intermittent hemodialysis
K+	Potassium
KC	Keratinocyte-derived chemokine
KIM-1.....	Kidney Injury Molecule-1
MCP-1	Monocyte chemo attractant protein-1
MDRD	Modification of Diet in Renal Disease
MPGN	Membranoproliferative glomerulonephritis
MRA	Magnetic resonance angiography
NE	Nor-Epinephrine
NGAL	Neutrophil Gelatinase-Associated Lipocalin
NHE3.....	Sodium/hydrogen exchanged isoform 3
PCI	Percutaneous coronary interventions
PD	Peritoneal dialysis
PSGN	Poststreptococcal glomerulonephritis

List of Abbreviations (Cont...)

RAD	Renal tubule assist device
RPGN	Rapid progressive glomerulonephritis
RRT	Renal replacement therapy
SCUF	Slow continuous ultrafiltration
SLED	Sustained low efficiency dialysis
THAM	Tris-hydroxy- methylaminomethane
TTP	Thrombotic Thrombocytopenic Purpura
UFH	Unfractionated heparin

List of Tables

List of Figures


بسم الله الرحمن الرحيم
إقرأ باسم ربك الذي
خلق ﴿١﴾ خلق الإنسان
من علق ﴿٢﴾ إقرأ وربك
الاكرم ﴿٣﴾ الذي علم
بالقلم ﴿٤﴾ علم الإنسان
ما لم يعلم ﴿٥﴾
صدق الله العظيم
سورة العلق
(الآيات (١-٥)

First of all, I am deeply grateful to *ALLAH*

I would like to express my deepest gratitude and appreciation to **Prof. Dr. Seif El-Islam Abd-ElAziz Shaheen,** Professor of Anesthesiology and Intensive Care, Faculty of Medicine, Ain shams University, for his kind guidance, continuous help and support through this work and it was a great honor to finish this work under his supervision.

I am very grateful to **Dr. Ahmed Mohammed El-Sayed El-Hennawy,** Assistant Professor of Anesthesiology and Intensive Care, Faculty of Medicine, Ain Shams University for his positive supervision during the preparation of this essay and for the extensive time and effort to offer every possible help to complete this work.

Special appreciation to **Dr. Abd-Alaziz Abd-Allah Abd-Alaziz,** Lecturer of Anesthesiology and Intensive Care, Faculty of Medicine, Ain Shams University for his kind advice, valuable instructions and continuous support which was the corner stone in the completion of this work.

Last but not least, I would like to present a lot of thanks to my *father*, *mother* and my *wife*, whose without their help and support, this work could not come to birth.

Ahmed Elsayed

INTRODUCTION

Intensive or critical care medicine is currently a well established medical specialty with specific therapies publications, practical and cognitive skills, and associated procedures. The evolution of the intensive care units (ICU) has had significant implications for clinical nephrologists especially in relation to the nature, epidemiology, and management of severe acute renal failure (ARF). Severe ARF, in fact, is now seen predominantly in ICUs ***(Bellemo et al., 2004).***

ARF is a clinical syndrome characterized by an abrupt decline in renal function resulting in an inability to excrete metabolic wastes and maintain proper fluid and electrolyte balance. In recent years, it has been recognized that the time honored term ARF fails to adequately describe what is a dynamic process extending across initiation, maintenance, and recovery phases, each of which may be of variable duration and severity. The alternative proposed term acute kidney injury (AKI) better captures the diverse nature of this syndrome, and has entered into widespread clinical use ***(Dennen et al., 2010 & Hoste and Kellum, 2010).***

Many definitions of AKI exist. These are typically based on either a fixed or relative increment in the serum creatinine level or reductions in urinary output. Recently, a new definition of AKI has been widely accepted. This scheme is referred to by

the acronym RIFLE, (Risk of renal dysfunction, Injury to the kidney, and Failure of kidney function and two outcome categories-Loss of function, and End stage kidney disease). Based on recent clinical studies, the increasing use of the RIFLE criteria is justified, as this approach appears to be a good method for both the diagnosis of and prognostication in ARF ***(Dennen et al., 2010 & Hoste and Kellum, 2010).***

In critically ill patients more than 90% of ARF episodes are of ischemic or toxic etiology or a combination of both. It is usually associated with dysfunction of other organ systems, often accompanied by sepsis and is typically multi factorial. Septic ARF is the most frequent and lethal cause of kidney failure in the intensive care unit (ICU). However, the precise diagnosis of the etiology of ARF is not always obvious or easy to establish ***(Hoste and Schurgers, 2008).***

Regardless of the underlying cause, AKI is associated with not only significantly increased in hospital morbidity, mortality and costs but also with a higher mortality risk in patients who survived for at least 90 days after hospital discharge ***(Vincent, 2007; Ricci et al., 2008 & Lafrance and Miller, 2010).***

Overall hospital mortality was more than 50% in the patients with AKI ***(Palevsky and Weisbord, 2009).***

Thus, the early detection and causal treatment of acute kidney problems is vitally important for a successful outcome. Although mortality rates have changed only modestly since the advent of hemodialysis, evidence suggests that comorbidities and illness severity have increased, masking real improvements in the care and outcomes for AKI ***(Cruz and Ronco, 2007).***

The percentage of patients with ARF who require renal replacement therapy (RRT) ranges from 20 to 60%. Among the subgroup of patients who survive initial dialysis, less than 25% require long term dialysis, demonstrating the potential reversibility of the syndrome ***(Jun et al., 2010).***

In the last decade,many papers on the use of new Urinary and serum biomarkers for AKI were published. Mostly concluding that these biomarkers will lead to a New era with earlier diagnosis, better prognostication of Outcome in terms of need for renal replacement and/or mortality,and finally better survival ***(Coca et al., 2008).***

The Neutrophil Gelatinase-Associated Lipocalin (NGAL) is a protein covalently bound to gelatinase in neutrophils which is usually expressed at very low concentrations in several human tissues, including kidney, lung, stomach, and colon ***(Mishra et al., 2003).***

NGAL was detected easily in the blood and urine soon after AKI in experimental and clinical studies ***(Kuwabara et al., 2009).***

Therefore, NGAL has proved an early, sensitive, non-invasive biomarker for AKI in different clinical settings such as in cardiac surgery,critical care and kidney transplantation ***(Wagener et al., 2008).***