

Adrenal Insufficiency In Critically Ill Patients

An Essay

Submitted for partial fulfillment of
Master Degree In Intensive care
By

Ibrahim Al Saeed Al Sangidy

M.B.,B,Ch

Faculty of Medicine – El-Mansoura University

Under Supervision of :

Prof. Dr. Magdy Mohamed Hussein Nafie

Professor of Anaesthesiology and Intensive Care,
Ain Shams University

Dr. Ihab Hamed Abd El Salam

Assistant Professor of Anaesthesiology and Intensive Care,
Ain Shams University

Dr. Ashraf El Saied Abd El Rahman El

Agamy

Lecturer of Anaesthesiology and Intensive Care,
Ain Shams University

**Faculty of Medicine
Ain Shams University**

2009

ACKNOWLEDGEMENT

I would like to express my gratitude to all those who gave me the possibility to complete this work.

*I am deeply indebted to my supervisor **Prof. Dr. Magdy Mohamed Hussein Nafie** Professor of Anaesthesiology and Intensive Care, Ain Shams University whose help, support, stimulating suggestions and encouragement helped me in all the time of research for and writing of this work.*

*I also would like to thank **Dr. Ihab Hamed Abd El Salam** , Assistant Professor of Anaesthesiology and Intensive Care, Ain Shams University who supported me in my work. I want to thank him for his help, support, interest and valuable hints*

*I also would like to thank **Dr. Ashraf El Saied Abd El Rahman El Agamy**, Lecturer of Anaesthesiology and Intensive Care, Ain Shams University, who supported me in my work. I want to thank him for his help, support, interest and valuable hints*

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Protocol

Elevation in corticosteroid level to meet physiological needs during acute illness is a protective response to stress. This homeostasis is maintained by the hypothalamic-pituitary-adrenal (HPA) axis. However, inadequate response as a result of corticosteroid insufficiency is common in critically ill patients, especially those with severe sepsis or septic shock. Thus, corticosteroids could be beneficial in the setting of septic shock or severe acute illness (*Jenn et al., 2008*).

It has been known since the mid 19th century that the adrenal cortex is essential for life. However, life-saving glucocorticoids replacement therapy for adrenal insufficiency (AI) was not widely available until the clinical introduction of cortisone in 1949. The initial standard of care established for glucocorticoids supplementation therapy during stress in hypoadrenal patients was based on early case reports of adrenal crises in patients not receiving adequate perioperative glucocorticoids coverage. Over the past decade, there has been a shift in clinical practice in favour of giving lower doses and shorter duration of glucocorticoids, according to the severity and duration of illness or surgery. The recommendations for glucocorticoids supplementation will provide useful information for physicians, anaesthetists, surgeons, dentists, obstetricians and general practitioners. (*Caroline and Warrick, 2008*).

During the acute phase of critical illness the hypothalamic-pituitary-adrenal (HPA) axis is activated, resulting in an increased cortisol production from the adrenal cortex. The degree of activation is proportional to the severity of disease, and it has been suggested that the assessment of HPA axis may have prognostic value. To

date the relationship to outcome of critically ill ICU patients has been investigated by basal cortisol or corticotropin (ACTH) stimulated cortisol levels. Both high and low basal cortisol concentrations have been associated with an adverse outcome. High cortisol levels reflect more severe stress, while low levels indicate an inability of the HPA axis to respond sufficiently to stress, suggesting that a properly functioning HPA axis is essential for survival. With regard to cortisol increases to ACTH a blunted response has been shown to constitute an independent predictor for poor outcome in some critical states including sepsis and systemic inflammatory response syndrome but not in others such as traumatic brain injury. The associations between cortisol patterns and outcome in mixed critically ill patients have not been well characterized. In particular the prognostic significance of cortisol levels after stimulation with synthetic ACTH in a general ICU population has received little systematic attention . (*Ioanna et al., 2007*).

Aim of the work

To discuss the problem of Adrenal Insufficiency (AI) in critically ill patients.

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- Anatomy of adrenal gland.
- Pathophysiology of adrenal gland.
- Adrenal Insufficiency in critically ill patients, a new look to an old problem
- Treatment of Adrenal Insufficiency in critically ill patients.

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List of Abbreviations

Abbreviation	Mean
ACTH	Adreno-Cortico-Tropic Hormone
AI	adrenal insufficiency
AIDS	Acquired Immune Deficiency Syndrome
AChE	acetyl cholinesterase
ARDS	Adult Respiratory Distress Syndrome
CIRCI	Critical illness-related corticosteroid insufficiency
CRH	corticotropin-releasing hormone
CABG	coronary artery bypass graft
DHEA	Di Hydroxy Epi Androsterone
DHEAS	dehydroepiandrosterone sulphate
HIV	Human Immunodeficiency Virus
HPA	hypothalamic-pituitary-adrenal

HD-ACTH test	High dose corticotropin stimulation test
IHT	Insulin-induced hypoglycemia test
ICU	Intensive care unit
LD-ACTH test	Low dose corticotropin stimulation test
RCTs	Randomized controlled trials
SD	Standard deviation
SIRS	Systemic Inflammatory Response Syndrome

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Introduction

Severe illness and stress activate the hypothalamic-pituitary-adrenal (HPA) axis and stimulate the release of corticotropin (also known as adrenal corticotrophic hormone [ACTH]) from the pituitary, which in turn increases the release of cortisol from the adrenal cortex. This activation is an essential component of the general adaptation to illness and stress, and contributes to the maintenance of cellular and organ homeostasis. Animals that have had adrenalectomies suffer rapidly to hemorrhagic and septic shock, and steroid replacement is protective against these challenges. Even minor degrees of adrenal insufficiency increases the mortality of critically ill or injured patients. Chronic primary adrenal insufficiency, as first described by Addison in the mid-1800s, is a rare disease. However, acute adrenal insufficiency is a common and largely unrecognized disorder in critically ill patients .

Over the last three decades , approximately 20 Randomized controlled trials (RCTs) have been conducted evaluating the role of glucocorticoids in patients with sepsis ,severe sepsis , septic shock , and ARDS .Varying doses (37.5 to 40,000 mg of hydrocortisone eq/day), dosing strategies (e.g. , single bolus, repeat boluses , continuous infusion ,and dose taper) and duration of therapy (1 to 32 days) were used in these studies .

The results of these studies together with the current understanding of Critical illness-related corticosteroid insufficiency (CIRCI) allow to make a number of general recommendations . It should be appreciated that the non stressed daily production of cortisol (hydrocortisone) in adults is approximately 15 to 25 mg/day, while the

maximal stressed daily production of cortisol (hydrocortisone) is approximately 200 to 350 mg/day .