The Differential Suppression Effect Of Maternal Adrenal Cortex In Women Receiving Single Versus Repeated Courses Of Antenatal Corticosteroids In Cases Of Preterm Birth

Thesis

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بسم الله الرحمن الرحيم

" قالوا سبحانك لاعلم لنا إلا ما علمتنا

إنك أنت العليم الحكيم"

صدق الله العظيم

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Abstract

Corticosteroids use in the management of preterm labour is no more controversial, it is a well-settled corner stone in the management of preterm labour to enhance fetal lung maturity.

Dexamethasone and betamethasone are used in this aspect successfully since 1972 but till now there was no settled protocol for the number of courses required to achieve optimum results.

In this study, no statistical difference was found between the 2 study groups regarding patient's age, gestational age and parity.

In our study maternal adrenal suppression was seen to be more prevalent among "the repeated courses group suggesting that multiple courses have profound suppressive action on hypothalarnic-piruitary-adrenal axis. So single course is much recommended.

Key words:

Pretermbirth (PTB) – ACTH – Corticosteroids – HPA .

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DEDICATION

To the spirit of my great father, my Wonderful Mother, my Son Ahmed and My Daughter Salma

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ACTH	Adrenocorticotropin hormone
AF	Amniotic fluid
CBG	Corticotropin binding globulin
CRH	Corticotropin releasing hormone
DIC	Disseminated intravascular coagulation
DPPC	Dipalmitoyl phosphatidyl choline (lecithin)
DHEAS	Dihydroepiandrostendione Sulphate
HMD	Hyaline membrane disease
HPA	Hypothalamic anterior pituitary axis
TRH	Thyroid Releasing Hormone
L/S	Licethin sphinogmylein
RDS	Respiratory distress syndrome
TTN	Transient Tachypnea of The newborn
Vs	Versus

INTRODUCTION

Preterm birth (PTB) is one of the leading causes of perinatal morbidity and mortality world wide ***(Saigal S., Doyle L.W., 2008)***.

It is defined as the presence of uterine contractions of sufficient frequency and intensity of effective progressive effacement and dilatation of the cervix prior to term gestation (between 20 and 37 wk). ***(Michael , 2009).***

Preterm birth and its consequences constitute a major health problem in the united states and worldwide. However there has been relatively little attention from the public research community despite the significant impact preterm birth has on infant mortality and subsequent disabilities of many survivals and on social and economic costs to the nation ***(Richard E, Behrmans, 2009)*** .

Preterm delivery complicate approximately 10% of all births, yet it accounts for more than three fourths of all neonatal deaths not associated with congenital anomalies ***(Johnson et al., 2003)***.

A woman at risk of preterm delivery is given a single course of 24 mg betamethasome doses, the question of whether repeated courses of corticosteroids would provide additional benefit and safe in women who remained undelivered 7 days of the initial course needs an answer.

However, evidence from several sources makes it clear that physicians do not wait for research to answer the question to the extent that many women receive weekly courses of corticosteroids as early as 24 wks ***(Banks et al., 1999)***. Among the potential hazards of repeated courses of corticosteroids is maternal adrenocortical suppression ***(Helal et al., 2006)***.

In a small study done by Dorr and Collegues have shown that maternal serum cortisol was significantly lower in women who had received intramuscular betamethasone compared to women who had not received antenatal steroids ***(Dorr et al., 1996)***. This conclusion was also reached by ***Charrnvises et al., 1995***, who assumed dose dependent adrenocortical suppression after injection of dexamethasone.

Another study done by ***Helal et al (2006)*** has found measurable adrenal suppression in women receiving repeated doses of antenatal corticosteroids when compared with those who did not receive steroids. These above studies have urged use to design a randomized trial with an acceptable number of patients comparing the suppressive effect of single and repeated courses of antenatal corticosteroids on the adrenal cortex.

AIM OF THE WORK

To compare the adrenocortical suppression effect of a single and repeated courses of dexamethasone for acceleration of fetal lung maturity in women with preterm birth.

Corticosteroids

They are a group of natural and synthetic analogues of the hormones secreted by the hypothalamic- anterior, pituitary (HPA) axis adrenocortical more commonly referred to as the pituitary gland. These include glucocorticoids, which are antiinflammatory agents with a large number of other functions; mineralocorticoids, which control salt and water balance primarily through action on the kidneys and corticotropins, which control secretion of hormones by the pituitary gland ***(Rietschel, Robert L, 2007)***.

Mechanism of action of corticosteroids:

Adrenocorticosteroids enter the cell where they combine with steroid receptors in the cytoplasm. The combination enter the nucleus where it controls the synthesis of proteins, including enzymes that regulate vital cell activities over a wide range of metabolic functions, as a consequence of the time requited for changes in gene expression and protein synthesis, most effects of corticosteroids are not immediate but become apparant after several hours ***(Laurance et al., 2005)***.

Regulation (control) of glucocorticoid secretion:

Glucocorticoid secretion is stimulated mainly by the adrenocorticotropic hormone (ACTH) that is secreted by the corticotrope cells of the anterior pituitary gland. ACTH is a single-chain polypeptide (containing 39 aminoacids) which maintains the structure, size and vascularity of the adrenal cortex. It stimulates

glucocorticoid and androgen secretion from both zona fasciculata and reticularis (but its effect on zona glomerulosa is minimal).

Mechanism of action o ACTH and control of its secretion:

In the adrenal cortex, ACTH acts by increasing the intraceullar cyclic AMP content in the target cells. Its secretion is controlled by 2 factors:

1- Corticotropin- releasing hormone (CRH):

It is secreted from the hypothalamus (figure 1), and it promotes ACTH synthesis and release from the corticotropes (by increasing the cyclic AMP content in these cells).

2- Feed back control:

A negative feedback relation exists between the free plasma glucocorticoids level and the secretion of ACTH. Such effect is produced at both the pituitary and hypothalamic levels (figure 1). Excessive ACTH secretion can also inhibit the release of CRH through a short loop feedback.

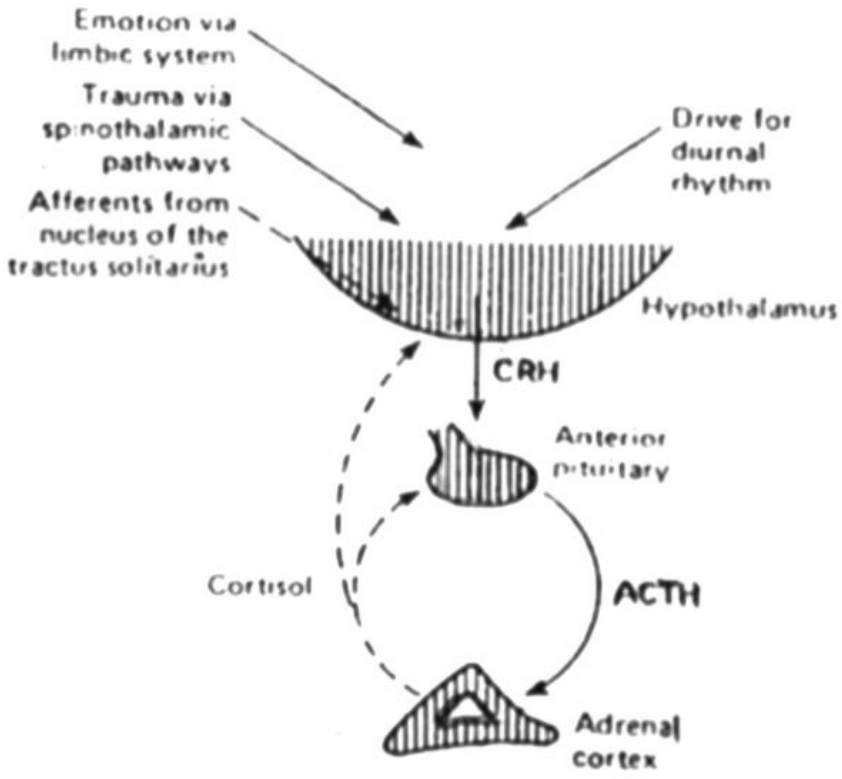

Fig. (1): Control of glucocrticoid secretion

ACTH response to stress:

Many stressful stimuli lead to secretion of ACTH (through stimulating CRH secretion from the hypothalamus e.g trauma or injury, anxiety, fear and other emotional stresses. Such stimuli excite many parts of the brain (especially the limbic system) which in turn stimulate the hypothalamic median eminence leading to CRH secretion.