EFFECT OF INTRA-MUSCULAR ADMINISTRATION OF DEXAMETHASONE ON THE DURATION OF INDUCTION OF LABOR IN PRIMIGRAVIDA FULL-TERM PREGNANCY

Thesis

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CONTENTS

LIST OF TABLES

LIST OF FIGURES

LIST OF ABBREVATIONS

11β-HSD1	11β-hydroxysteroid dehydrogenase
AC	Abdominal circumference
ACOG	American Congress of Obstetricians and Gynecologists
ACTH	Adrenocorticotropic hormone
ADD	Actual date of delivery
AFI	Amniotic fluid index
AGA	Average for gestational age
AP	Activating protein
AR	Androgen receptor
ARM	Artificial rupture of membrane
BMI	Body mass index
BP	Blood pressure
BPM	Beats per minute
BPP	Biophysical profile
CL	Cervical length
COX	Cyclooxygenase
CRH	Corticotrophin releasing hormone
CRH-BP	CRH-binding protein
CRH-R	CRH receptors
CS	Cesarean section
CSF	Colony stimulating factor
CST	Contraction stress test
CTG	Cardiotocography
CYP17	Cytochrome P450, 17alpha-hydroxylase/17, 20-lyse
DCs	Dendritic cells
DHEA-S	Dehydroepiandrosterone sulfate
DZ/TZ	Definitive/transitional zone
EASI	Extra-amniotic saline infusion
EFW	Estimated fetal weight
FDA	Food and Drug Administration
FGR	Fetal growth restriction
FH	Fundal height
FHR	Fetal heart rate
GBS	Group B streptococci
GCs	Glucocorticoids
GR	Glucocorticoid receptor
GRE	Glucocorticoid responsive elements
H.S.	Highly significant
HFA	Human fetal adrenal

HPA	Hypothalamic pituitary adrenal
HSD3B2	3-hydroxysteroid dehydrogenase type ЦI
IL	Interleukin
IOL	Induction of labor
IUFD	Intrauterine fetal demise
IUGR	Intrauterine growth restriction
LMP	Last menstrual period
MAS	Meconium aspiration syndrome
m-RNA	Messenger-RNA
MSL	Meconium stained liquor
N.S.	Non-significant
NICE	National institute for health and care excellence
NICU	Neonatal intensive care unite
NK T cells	Natural killer T cells
NO	Nitric oxide
NST	Non-stress test
PE	Pre-eclamsia
PGDH	Prostaglandin dehydrogenase
PGs	Prostaglandins
PIH	Pregnancy induced hypertension
PPH	Postpartum hemorrhage
PPROM	Preterm pre-labor rupture of membrane
PR	Progesterone receptor
PROM	Pre-labor rupture of membrane
RCOG	Royal College of Obstetricians and Gynecologists
RCTs	Randomized controlled trials
RDS	Respiratory distress syndrome
RLN	Relaxin
SD	Standard deviation
SGA	Small for gestational age
SP-A	Surfactant Protein-A
SVD	Spontaneous vaginal delivery
TNF	Tumor necrosis factor
TVU	Trans-vaginal ultrasound
US	Ultrasonographic
WHO	World health organization
β-AR	β-adrenergic receptor
μg	microgram

ABSTRACT

Objectives: to evaluate the effect of dexamethasone on labor duration and to establish whether dexamethasone plays a role in shorting the duration interval between initiation of labor induction and beginning of the active phase of labor in primigravida full-term pregnancy.

Study design: Case control study included 120 primigravidae with full-term pregnancy classified into two groups: group I (cases) included 60 women assigned to receive a single 8-mg dose of dexamethasone intra-muscular and group II (control) included 60 women will not receive dexamethasone or any other cervical ripening agent.

Results: The interval between initiation of labor induction and beginning of active phase of labor was shorter in the dexamethasone than in the control group **(2.54±0.94 hours vs. 3.59±0.86 hours; p=0.001).** Dexamethasone group shows shorter duration of active phase of labor than control group **(4.82±0.56 hrs. vs. 5.12±0.58 hrs.)**. Dexamethasone group shows shorter duration of first stage of labor than control group **(7.35±1.15 hrs. vs. 8.69±1.09 hrs.)**. Dexamethasone group shows faster rate of cervical dilatation than control group **(1.37±0.18 cm/hr. vs. 1.28±0.17 cm/hr.)**. Dexamethasone group shows shorter duration of second stage of labor than control group **(25.09±12.99 minutes vs. 30.73±12.96 minutes).** Oxytocin requirement in dexamethasone group was less than in control group **(5.35±1.49 hrs. vs. 5.97±1.34 hrs.).**

Conclusions: The administration of dexamethasone found to shorten labor duration.

KEYWORDS:
Dexamethasone; post-term pregnancy; induction of labor.

INTRODUCTION

Induction of labor refers to the process of artificially initiating uterine contractions prior to their spontaneous onset to effects progressive effacement and dilatation of the cervix and ultimately, delivery of the baby ***(Hayman, 2010).***

Induction of labor is one of the most common interventions practiced in modern obstetrics. In the developed World, the ability to induce labor has contributed to the reduction in maternal and perinatal mortality and morbidity ***(Subramanian and Penna, 2009).***

The goal of labor induction is to stimulate uterine contractions before the spontaneous onset of labor, resulting in vaginal delivery. The benefits of labor induction must be weighed against the potential maternal and fetal risks associated with this procedure. When the benefits of expeditious delivery are greater than the risks of continuing the pregnancy, inducing labor can be justified as a therapeutic intervention ***(Barclay, 2009).***

The success of induction and labor progression is dependent on the condition of the cervix before induction initiation ***(Barclay, 2009).***

In primigravidae, the mean time taken from induction to delivery is between 15 and 20 hours, of which up to 12 hours is spent in the cervical ripening phase before labor itself starts (***Stitely et al., 2000).***

About 10 percent of pregnancies may be prolonged. In general, the longer the truly post-term fetus stays in the uterus, the greater the risk of a severely compromised fetus and newborn infant. Therefore of major importance in handling compromised postdate pregnancies is the use of a suitable method of labor induction ***(Petraglia et al., 2003).***

A prolonged gestation is more likely to occur when the fetus has congenital adrenal hyperplasia caused by 2l-hydroxylase deficiency, which may be due to an impaired cortisol production ***(O'Sullivan et al., 2007).***

Glucocorticoids are now known to play key roles in fetal maturation for example in maturation of the lung in anticipation of extra-uterine life and in several species appear to be mediators in the initiation of labor. In humans, the placenta synthesizes CRH, and the exponential rise of this hormone in maternal plasma correlates with the timing of birth ***(Falah N et al., 2014).***

Glucocorticoids derived from the maturing fetal hypothalamus-pituitary-adrenal axis play a crucial role in triggering parturition ***(Challis et al., 2005).***

Different studies have shown the paracrine and autocrine effects of corticosteroids on the human uterus, and receptors for these agents have been detected on the human amniotic membranes ***(Kavanagh et al., 2006).***

The corticotrophin-releasing hormone (CRH), which has been identified in various organ systems, including the female reproductive system, is the principal regulator of the hypothalamic-pituitary-adrenal axis. Circulating placental CRH is responsible for the physiologic hypercortisolism of the latter half of pregnancy and plays a role in the onset of labor ***(Kalantaridou et al., 2007).***

During pregnancy, large amounts of CRH are released from the placenta and fetal membranes. An increment in plasma CRH concentration occurs during spontaneous labor, with peak value at vaginal delivery ***(Riley & Challis, 2003).*** Placental CRH is also released into the fetal circulation, dehydroepiandrosterone and in vitro CRH directly stimulates sulfate (DHEA-S) production from the fetal zone of the fetal adrenal ***(Sirianni et al., 2005).***

This increase in fetal zone activity correlates with rising levels of maternal estrogen levels through the conversion of DHEA-S to estrogens within the placenta. The increase in the maternal estrogen to progesterone ratio may promote the expression of contraction-associated proteins in the myometrium, thus facilitating the initiation of parturition ***(Mastorakos and Ilias, 2003).***

Cortisol increases the production of prostaglandins in the fetal membranes by either up regulating prostaglandin synthesis (PGHS-2) levels or down regulating 15-hydroxy prostaglandin dehydrogenase (PGDH) ***(Patel et al., 1999***).

It has been very well recognized that increased prostaglandin (PGE_2 and PGF_2) biosynthesis as a result of inflammation-like responses in intrauterine tissues is one of the key events leading to parturition in both term and preterm human labor because these compounds evoke uterine contractions as well as cervical softening and effacement ***(Kang et al., 2006).***

Human fetal membranes are generally regarded as the major sources of prostaglandins at the end of pregnancy. However, it is not clear whether SP-A affects prostaglandin synthesis in human fetal membranes ***(Kang et al., 2006).***

Therefore, glucocorticoids also play an important role in human parturition. This cascade of events initiated by glucocorticoids may play an important role in the positive feed-forward mechanisms.

AIM OF THE WORK

To establish whether a single dose of dexamethasone (8mg) intra-muscularly plays a role in shorting the duration interval between initiation of labor induction and beginning of the active phase of labor in primigravida full-term pregnancy.

CHAPTER 1

GLUCOCORTICOIDS AND HUMAN PARTURITION

Hormones normally produced by the adrenal cortex include hydrocortisone (cortisol) and some androgens and estrogens; the synthesis and release of which is controlled by the hypothalamic-pituitary system, and aldosterone, whose biosynthesis is largely dependent on the renin-angiotensin system ***(Diana, 2012).***

The glucocorticoids have widespread actions on intermediate metabolism, affecting carbohydrate and protein metabolism as well as a potent regulatory effect on our endogenous 'defense' reactions such as the innate and acquired immune response. The adrenal gland secretes a mixture of glucocorticoids, but the main hormone in humans is hydrocortisone (also, confusingly, called cortisol), but in rodents corticosterone predominates ***(Rang et al., 2012).***

Positive feedback loop involving glucocorticoids, pro-inflammatory cytokines, prostaglandins (PGs), surfactant protein-A (SP-A) and 11β-hydroxysteroid dehydrogenase (11β-HSD1) is formed locally in human fetal membranes towards term or in preterm labor. This positive feedback loop would produce abundant biologically active glucocorticoids and PGS in fetal membranes or amniotic fluid, which would ultimately promote fetal organ maturation and initiate parturition ***(Myatt and Sun, 2010).***

Synthesis:

The hormones of the adrenal cortex are steroids derived from cholesterol. The rate-limiting step in adrenal hormone biosynthesis is the modification of cholesterol to pregnenolone by side-chain cleavage enzyme. From this step, pregnenolone metabolism can be directed toward the formation of aldosterone, cortisol, or androstenedione. The flux of