Effect of Intramuscular Administration of Dexamethasone on the Duration of Labor: Randomized Controlled Trial

A Thesis

Submitted For Partial Fulfillment of Master Degree
in Obstetrics and Gynecology

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2017

Acknowledgments

First and foremost, I feel always indebted to Allah, the Most Beneficent and Merciful. I can do nothing without Him.

I would like to express my sincere gratitude to* Prof. Hatem El Gamal,** ***Professor of Obstetrics and Gynecology, Faculty of Medicine – Ain Shams University,, under his supervision, I had the honor to complete this work, I am deeply grateful to him for his professional advice, guidance and support.

My deep gratitude goes to* Dr. Mohamed Abd El Aleem,** ***Lecturer of Obstetrics and Gynecology, Faculty of Medicine – Ain Shams University, for his great support, tireless guidance and meticulous supervision throughout this work.

Last but not least, I like to thank all my Family, especially my Parents and my Wife, for their kind care, help and encouragement.

Michael Farah Sadek

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List of Abbreviations

Abbr.	Full-term
ACTH	**:** Adrenocorticotropic hormone
BMI	**:** Body mass index
c-AMP	**:** Cyclic adenosine monophosphate
CAPs	**:** Contraction-associated proteins
COX-2	**:** Cyclooxygenase 2
CRH	**:** Corticotropin-releasing hormone
DHEAS	**:** Dehydroepiandrosterone sulfate
EASI	**:** Extra-amniotic saline infusion
fFN	**:** Fetal Fibronectin
HFA	**:** Human fetal adrenal
IGFBP	**:** Insulin-like growth factor binding protein
PG	**:** Prostaglandins
PGDH	**:** Prostaglandin dehydrogenase
PGHS	**:** Prostaglandin synthesis
SD	**:** Standard deviation
SPSS	**:** Statistical package for social science

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ABSTRACT

Background: Prostaglandins (PG F2 and PG E2) have long been involved in the spontaneous onset of labor. The normal process of labor appear to result in inflammation which result in increased prostaglandin synthesis, Prostaglandins produced in myometrial tissue contribute to the effectiveness of myometrial contractions during labor and may soften the cervix independent of uterine activity. **Aim of the Work:** The aim of this work is to assess the effect of intramuscular administration of dexamethasone on the progress and the duration of labor. **Patients and Methods:** This randomized, double-blind, controlled study was conducted in Ain Shams University Maternity Hospital. A total of 140 women undergoing induction of labor were included in this study after taking their consent for this clinical trial after full explanation of the trial. **Results:** Shorter duration from initiation of labor induction to beginning of active phase of labor than control group Dexamethasone group shows shorter duration of first stage of labor than control group. There was a high significant statistical difference between the two groups as regard first stage of labor of labor ($p<0.001$). **Conclusion:** The administration of 8 mg dexamethasone intramuscular during induction of labor is a simple applicable method to shorten the duration of labor. **Recommendations:** Further researches with more patients needed for the assessment of the effects of the corticosteroids on the duration of labor on the patients with unfavorable cervix. Further researches needed for the assessment of maternal and perinatal morbidity and mortality rate.

Key words: dexamethasone, labor, intramuscular administration

Introduction

The last few hours of human pregnancy are characterized by uterine contractions that affect cervical dilatation and cause the fetus to descend through the birth canal; these forceful painful contractions are preceded by extensive preparations in both the uterus and cervix. During the first 36 to 38 weeks of normal gestation the myometrium is in a preparatory, yet unresponsive state concurrently the cervix begins an early stage of remodeling termed softening yet maintains structural integrity following this prolonged uterine quiescence, there is a transitional phase during which myometrial unresponsiveness is suspended and the cervix undergoes ripening effacement, and loss of structural integrity ***(Mendelson, 2009).***

The physiological process that regulates parturition and the onset of labor continue to be defined. It is clear however that labor onset represents the culmination of a series of biochemical changes in the uterus and cervix. These result from endocrine and paracrine signals emanating from both mother and fetus. Their relative contributions vary between species and it is these differences that complicate elucidation of the exact factors that regulate human parturition ***(Cunningham et al., 2010)***

Prostaglandins particularly (PG F2 and PG E2) have long been involved in the spontaneous onset of labor. The normal process of labor appears to result in inflammation which results in increased prostaglandin synthesis, Prostaglandins produced in myometrial tissue contribute to the effectiveness of myometrial contractions during labor and may soften the cervix independent of uterine activity ***(Yu-Hsin et al., 2012).***

Induction of labor refers to iatrogenic stimulation of uterine contractions to accomplish delivery prior to the onset of spontaneous labor. It is one of the most commonly performed obstetrical procedures ***(Robinson., 2017).***

Labor may be induced for either maternal or fetal indications. Induction of labor is undertaken when continuing the pregnancy is believed to be associated with greater maternal or fetal risk than intervention to deliver the pregnancy, and there is no contraindication to vaginal birth ***(ACOG, 2009).***

Labor induction with prostaglandin F2 alpha was known since 1960. Subsequently, formulations of prostaglandin E2 (PGE2, dinoprostone) were developed which largely replaced the use of F2 alpha ***(Rugarn et al., 2017).***

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) ***(Smith, 2007).***

Glucocorticoids are now known to play key role in fetal maturation of the lung in anticipating of extra uterine life and in several species appear to be mediators in the initiation of labor ***(Myatt & Sun, 2010).***

In Humans, the placenta synthesizes CRH and the exponential rise of this hormone in maternal plasma correlates with the timing of birth ***(Norwitz et al., 2015).***

Also glucocorticoids induce the production of CRH by the placenta and the production of prostaglandins (PGF2 & PGE2) by the fetal membranes in human ***(Cheng et al., 2010).***

A large number of glucocorticoids analogues have been synthesized including dexamethazone, prednisolone, pridnesone and fludrocortisones ***(Adler & Garg, 2012).***

Dexamethazone – a synthetic glucocorticoid – may decrease the duration of labor by increasing the production of prostaglandins in the fetal membranes which contributes to the effectiveness of myometrial contractions during labor and may soften the cervix independent of uterine activity ***(Marciniak et al., 2012).***

Aim of the Work

The aim of this work is to assess the effect of intramuscular administration of dexamethasone on the progress and the duration of labor.

Research question:

Does the administration of intramuscular dexamethasone during induction of labor affect the progress and the duration of labor?

Research hypothesis:

The administration of intramuscular dexamethasone during induction of labor may shorten the duration of labor.

Physiology of Labor

Labor is a physiological event involving a sequential, integrated set of changes within the myometrium, decidua and uterine cervix that occur gradually over a period of days to weeks. Biochemical connective tissue changes in the uterine cervix appear to precede uterine contractions and cervical dilation, and all of these events usually occur before rupture of the fetal membranes. Labor is a clinical diagnosis, which includes: (1) the presence of regular phasic uterine contractions increasing in frequency and intensity, and (2) progressive cervical effacement and dilatation ***(Norwitz et al., 2015).***

The physiological processes that regulate parturition and the onset of labor continue to be defined. It is clear, however, that labor onset represents the culmination of a series of biochemical changes in the uterus and cervix. These result from endocrine and paracrine signals emanating from both mother and fetus. Their relative contributions vary between species, and it is these differences that complicate elucidation of the exact factors that regulate human parturition ***(Cunningham et al., 2010).***

Causes of onset of labor (Theories)

The exact mechanism, by which labor is started spontaneously, at either term or preterm, is unknown. Many theories have been proposed.

A- Oxytocin stimulation:

Endogenously produced oxytocin, which causes uterine contractions, may play a role in the spontaneous onset of labor. Levels of oxytocin in maternal blood in early labor are higher than before the onset of labor, but there is no evidence of a sudden surge. Oxytocin influence must therefore rely on the presence of oxytocin receptors. Receptors are found in the nonpregnant uterus ***(Norwitz et al., 2015)***

There is a six fold increase in receptors at 13 to 17 weeks' gestation and an 80-fold increase at term.The increased number of oxytocin receptors amplifies the biologic effect of oxytocin, and contractions intensity ***(YU-HSIN, 2012).***

B- Fetal cortisol levels:

Fetal cortisol levels may influence the spontaneous onset of labor. Disruption of hypothalamic–pituitary–adrenal axis or the absence of adrenal gland or function results in prolonged gestation in humans and sheep. In sheep, infusion of cortisol or ACTH into a fetus with an intact adrenal gland causes premature labor. However, in humans, there has been no documentation of prelabor surge in fetal cortisol secretion to completely support this theory ***(YU-HSIN, 2012).***

C- Progesterone withdrawal:

In rabbits, the withdrawal of progesterone is followed by the prompt evacuation of the contents. In humans, there is no obvious decrease in maternal blood levels of progesterone at term or in labor. However, the progesterone level at the placental site may decrease before the onset of labor. This decrease in progesterone, in association with increased estrogen levels, is followed by increased formation of gap junctions, which permit coupling of the myometrial cells ***(YU-HSIN, 2012).***

D- Prostaglandin release:

Prostaglandins, particularly PGF 2(alpha) and PGE2, have long been believed to be involved in the spontaneous onset of labor. The normal processes of labor appear to result in inflammation, which results in increased prostaglandin synthesis. Prostaglandins produced in myometrial tissue may contribute to the effectiveness of myometrial contractions during labor, and may soften the cervix independent of uterine activity ***(YU-HSIN, 2012).***

Maternal–fetal interactions

In the intervillous space, the syncytiotrophoblasts release corticotropin-releasing hormone (CRH), progesterone, and estrogens into the maternal blood and into the fetal blood. Cortisol passes through a maternal artery and enters the