Role of Dexamethasone in Induction of Labor:
(A Randomized Clinical Trial)

Thesis

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Kareem Medhat

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List of Abbreviations

Abb.	Full term
11ß-HSD	11ß-hydroxysteroid dehydrogenase
ACTH	Adrenocorticotropic hormone
AUGR	Intrauterine growth restriction
BMI	Body mass index
c-AMP	Cyclic adenosine monophosphate
Cox-2	Cyclooxygenase 2
CPD	Cephalopelvic disproportion
CRH	Corticotropin-releasing hormone
CTG	Cardiotocography
DBP	Diastolic blood pressure
DHEAS	Dehydroepiandrosterone sulfate
EASI	Extra-amniotic saline infusion
fFN	Fetal Fibronectin
FHR	Fetal heart rate
GA	Gestational age
HFA	Human fetal adrenal
IGFPB-1	Insulin-like growth factor binding protein-1
LMP	Last menstrual period
PG	Prostaglandins
PGDH	Prostaglandin dehydrogenase
PGHS-2	Prostaglandin endoperoxide synthase 2
SBP	Systolic blood pressure
SD	Standard deviation
SPSS	Statistical package for social science

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Role of Dexamethasone in Induction of Labor:

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Abstract

Background: Labor induction is a common obstetric procedure which is done for many indications. Ripening of the cervix is a complex process involving hormonal, vasodilatory and inflammatory changes. There are broad range of methods for cervical ripening and induction of labor. **Aim of the study: to** assess the efficacy of intramuscular administration of dexamethasone on the induction delivery-interval in full term women undergoing induction of labor. **Patients and Methods**: This study was carried out between July 2018 and January 2019, at the labor ward of Ain Shams university maternity hospital, a double bind randomized control trial of 80 pregnant women undergoing induction of labor after obtaining the approval of the local ethical committee and a fully-informed written consent. They were randomized into two groups: group D (Dexamethasone group n=40) and group C (control group n=40). **Results:** Of 80 pregnant women undergoing induction of labor there were no statistically significant differences between the two groups as regard their age, body mass index, gestational age and bishop score at time of intervention. There was significant statistical difference between the two groups as regard induction-active phase interval ($P < 0.05$), mean induction-active phase interval in group D was (4.91±.85 hours) while in group C was (5.44±.83 hours). There was no significant statistical difference between the two groups as regard duration of active phase of labor, mean duration of active phase in group D was (4.10±.97 hours) and in group C (4.47±1.20 hours). There was significant statistical difference between the two groups as regard induction-delivery interval ($P < 0.05$), mean induction-delivery interval in group D was (9.73±.1.52hours) while in group C was (10.70±1.87 hours). There were no statistically significant differences between the two groups as regard duration of 2nd and 3rd stages of labor. **Conclusion:** Single intramuscular injections of 2 ml. (8mg) of dexamethasone before induction of labor seems to shorten induction-delivery interval by shortening the induction-active phase interval.

Keywords: Induction of labor, Duration of labor, Dexamethasone, Corticosteroids, Prostaglandins

PROTOCOL OF A THESIS FOR PARTIAL FULFILMENT OF MASTER DEGREE IN OBSTETRICS & GYNAECOLOGY

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What is already known on this subject? AND
What does this study add?

The use of corticosteroids is one of the methods put forward for the strengthening and speeding up the process of labor. After identification of glucocorticoid receptors in human amnion, the role of corticosteroids in starting the process of labor has been studied in numerous studies. Some of them discussed the relation between dexamethasone injection and labor induction but still there is insufficient data. So by the end of this study it may be possible to assess the effect of intramuscular dexamethasone injection on shortening the induction delivery interval.

1.INTRODUCTION/ REVIEW (maximum 1000 words)

Labor is the last few hours of human pregnancy. It is characterized by forceful and painful uterine contractions that effect cervical dilation and cause the fetus to descend through the birth canal. Extensive preparations take place in both the uterus and cervix long before this. 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 yet maintains structural integrity. Following this prolonged uterine quiescence, a transitional phase follows during which myometrial unresponsiveness is suspended and the cervix undergoes ripening, effacement, and loss of structural cohesion ***(Cunningham et al., 2016).***

Cervical ripening is a complex process involving extensive remodeling and dynamic anatomic and physiologic alterations governed by hormonal changes, inflammatory responses, vasodilatory changes, and other biological processes. Prostaglandins, produced both locally in the cervix and uterus as well as originating from the fetal membranes, play a critical role in cervical ripening and uterine contractility by increasing inflammatory mediators in the cervix and inducing cervical remodeling ***(Bakker et al., 2017).***

Induction of labor is a common obstetric procedure which is performed for a variety of medical and non medical indications ***(Schwarz et al., 2016).*** Induction of labor is the process by which labor is started prior to its spontaneous onset by artificial stimulation of uterine contractions and/or progressive cervical effacement and dilatation, leading to active labor and birth. The clinical need for induction of labor occurs when it is perceived that the outcome of the pregnancy will be improved if it is interrupted by induction, labor and birth ***(Luesly and Kilby, 2016).***

There is a broad range of methods available for induction of labor. The choice of method may depend on national guidelines and local protocol, as well as individual clinical factors but prostaglandins particularly PGE1 and PGE2 remain a preferred method for cervical ripening and labor induction ***(Schwarz et al., 2016)***.

Overall, misoprostol and oxytocin with amniotomy is more successful than other agents in achieving vaginal delivery within 24 hours ***(Alfirevic et al., 2016).***

The mechanisms involved in human pregnancy and parturition are highly complex and involve mother, fetus and placenta. The final common pathway to delivery is composed by inflammatory and endocrine interactive paths that tip the balance in favor of coordinated uterine contractility and cervical dilation ***(Vannuccini et al., 2016).***

In most mammalian species, there is an increase in glucocorticoid concentration in maternal and fetal circulations as well as in amniotic fluid towards the end of gestation and at the onset of labor. This surge of glucocorticoids is believed to be crucial to maturation of fetal organs as well as to be integral to the cascade of events in the initiation and maintenance of labor ***(Li et al., 2014).***

Steroid substances produced in the adrenal glands of the human fetus affect the placenta and the membranes and transform the myometrium from the static to the contractile state, The placenta may play a role in this process because it produces a lot of CRH

(Corticotropin releasing hormone). The adrenal glands of the fetus do not produce a considerable amount of cortisol until the third trimester. During the last weeks of pregnancy, the cortisol and DHEA–S (Dehydroepiandrosterone sulfate) contents of the fetus rise and this leads to an increase in maternal estrogens, a particularly sterol. The concentration of CRH in the fetus rises during the last 12 weeks of pregnancy. This results in modification of the contractility of the uterus, stimulation of the membranes to produce more prostaglandins, stimulation to produce C19 steroids from placental adrenaline, and increase in the estrogen content ***(Laloha et al., 2015).***

A large number of Steroid analogues have been synthesized including dexamethazone, prednisolone, pridnesone and fludrocortisones ***(Samuel et al., 2017).***

Dexamethasone is a synthetic glucocorticoid that is commonly used in human medical practice as potent anti-inflammatory, immunosuppressive and analgesic agent. In pharmacological doses, it plays a major role in the treatment of many diseases ***(Yahi et al., 2017).***

Studies have shown that corticosteroids analogues as dexamethasone could improve the Bishop score of the cervix and thus causes softening of the cervix and reduces the length of time between labor induction and delivery but further studied in that field is still needed ***(Laloha et al., 2015).***

2.AIM / OBJECTIVES

Research hypothesis:

In pregnant women undergoing induction of labor, intramuscular injection of dexamethasone may accelerate induction delivery interval.

Research question:

In pregnant women undergoing induction of labor, does intramuscular injection of dexamethasone accelerate induction delivery interval?

This study aims to assess the effect of intramuscular administration of dexamethasone on the induction delivery interval in full term patients undergoing induction of labor.

3.METHODOLOGY:

Patients and Methods/ Subjects and Methods/ Material and Metho

- **Type of Study:** Randomized Clinical Double Blind Trial.
- **Study Setting:** The study will be conducted at Ain Shams Maternity Hospital.
- **Study Population:** Full term patients who attend to the labor ward in El Demerdash Maternity Hospital and scheduled for induction of labor.
- **Sampling Method:** Convenience sampling
- **Sample Size:** Sample size was calculated using PASS® version 15.0, setting the power (β) at 0.02 and the significance level (α) at 0.05. Data from previous reports **(Kashanian et al., 2008)** indicated that mean Induction-Active phase Interval in women receiving 8mg of dexamethasone before induction of labor and controls was 3.09±1.5 and 4.21±1.8 hours respectively. Calculation according to these values produced a minimal sample size of 70 patients to be randomized equally to both groups. Assuming a drop-out rate of 15%, a minimum drop-out inflated enrollment sample size of approximately 80 women will be needed.
- **Ethical Considerations:** The study will be approved from the Ethical Committee of the Department of Obstetrics and Gynecology, Faculty of Medicine, Ain Shams University.

Informed written consent will be taken from all women before recruitment in the study, and after extensive explanation and clear discussion of risks and benefits.

- **Study Procedures:** A total of 80 women undergoing induction of labor will be included in this study after taking their consent for this clinical trial after full explanation of the trial.

Grouping: The total of 80 included patients will be distributed into two groups:

- Group D (Study group-Dexamethasone group) :

Forty patients undergoing induction of labor will receive 8 mg (2ml) of the product dexamethasone sodium phosphate intramuscular one hour before the initiation of labor induction in the form of epidrone® ampoules which is a dexamethasone product from Epico-Egypt, and labor induction will be performed according to the American College of Obstetricians and Gynecologists protocol, i.e, starting by 25 mcg of PGE1 vaginally, in the form of Vagiprost®, every 3-6 hours according to patient response, Dexamethasone will be given one hour before the first dose of Vagiprost, when bishop score reaches 6 to 8, oxytocin will be added by 5 drops/minute of 500 cc saline + 5 units of oxytocin with the dose increasing by 5-10 drops / minute every 30 minute till optimal contractions are reached which are three uterine contractions in 10 minutes and each lasting for 40-50 seconds ***(ACOG, 2017).***

Any complications of induction such as fetal bradycardia, cord prolapse or even failed induction after four doses of vagiprost®, patient will delivered by doing cesarean section and will be dropped out from the study.

- Group C (Control group):

Forty patients undergoing induction of labor will receive 2ml of normal saline intramuscular one hour before the initiation of labor induction, and labor induction will be performed by the same protocol as above.