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EFFECT OF INTRAMUSCULAR ADMINISTRATION OF DEXAMETHASONE ON THE DURATION OF LABOR INDUCTION

Thesis

Submitted for Partial Fulfillment of Master Degree in Obstetrics and Gynaecology

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Wafaa Ahmed Abdelsalam

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List of Abbreviations

11ß-HSD1	*11ß-Hydroxy steroid dehydrogenase type1*
ACOG	*American College of Obstetricians and Gynecologists*
ACTH	*Adrenocorticotrophic hormone*
AFI	*Amniotic fluid index*
ATP	*Adenosine triphosphate*
BMI	*Body mass index*
BP	*Blood pressure*
BPM	*Beats per minute*
BPP	*Biophysical profile*
C/S	*Cesarean Section*
c-AMP	*Cyclic adenosine monophosphate*
cc	*Cubic centimeters*
COX-2	*Cyclooxygenase 2*
cPLA2	*Cytosolic phospholipase A2*
CRH	*Corticotrophin Releasing Hormone*
CRH-BP	*CRH-binding protein*
CSF	*Colony-stimulating factor*
CST	*Contraction stress test*
cyclic AMP	*Cyclic adenosine monophosphate*
CYP17- CYP11A	*Cytochrome enzyme (p17-p11A)*
DHEAS	*Dehydro epiandrosterone sulfate*
DZ	*Definitive zone*
EASI	*Extra-Amniotic Saline Infusion*
EDD	*Expected delivery date*
EFM	*Electronic fetal heart rate monitoring*
Eg	*Example*
fFN	*Fetal Fibronectin*
FHR	*Fetal heart rate*
HFA	*Human fetal adrenal*
HSD3B2	*3-hydroxysteroid dehydrogenase type II*
IGFBP-1	*Insulin-Like Growth Factor Binding Protein-1*

IL-8	*Interleukin -8*
LMP	*Last menstrual period*
m2	*meters square*
M-CSF	*Macrophage stimulating factor*
MMPs	*Metallo proteinases*
mRNA	*Messenger Ribonucleic Acid*
NA	*Not applicable.*
NO	*Nitric oxide*
NST	*Non stress test*
PGDH	*15-hydroxy prostaglandin dehydrogenase*
PGE2-PGF2	*Prostaglandin*
PGHS	*Prostaglandin endoperoxide H synthase enzyme*
PGHS-2	*Prostaglandin synthesis*
PGs	*Prostaglandins*
RCOG	*Royal Colleague of Obstetrics and Gynecology*
SVD	*Spontaneous vaginal delivery*
TNF	*Tumor necrosis factor*
TZ	*Transitional zone*
WHO	*World Health Organization*

AIM OF THE WORK

The aim of this work is to evaluate the effect of intramuscular administration of dexamethasone on the progress and duration of phases of vaginal delivery during labor induction.

PARTURITION

The last few hours of human pregnancy are characterized by uterine contractions that effect 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 **(Cunningham et al., 2010).**

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).**

Theories of the causes of labor

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.

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 intervillous space, where it stimulates the production of CRH by the syncytiotrophoblasts. A fetal umbilical vein carries CRH into the fetal circulation, stimulating the fetal pituitary to synthesize corticotrophin and drive fetal adrenal cortisol and dehydroepiandrosterone sulfate (DHEAS) synthesis. Cortisol and CRH stimulate the fetal lungs to produce surfactant protein A, which moves from the amniotic fluid to the amnion, where it stimulates the production of cyclooxygenase 2 (COX-2) and the synthesis of prostaglandin E2. They pass along the chorion and decidua and stimulate the underlying maternal myometrial cells to synthesize additional COX-2 and prostaglandin F2α **(Smith, 2007).**

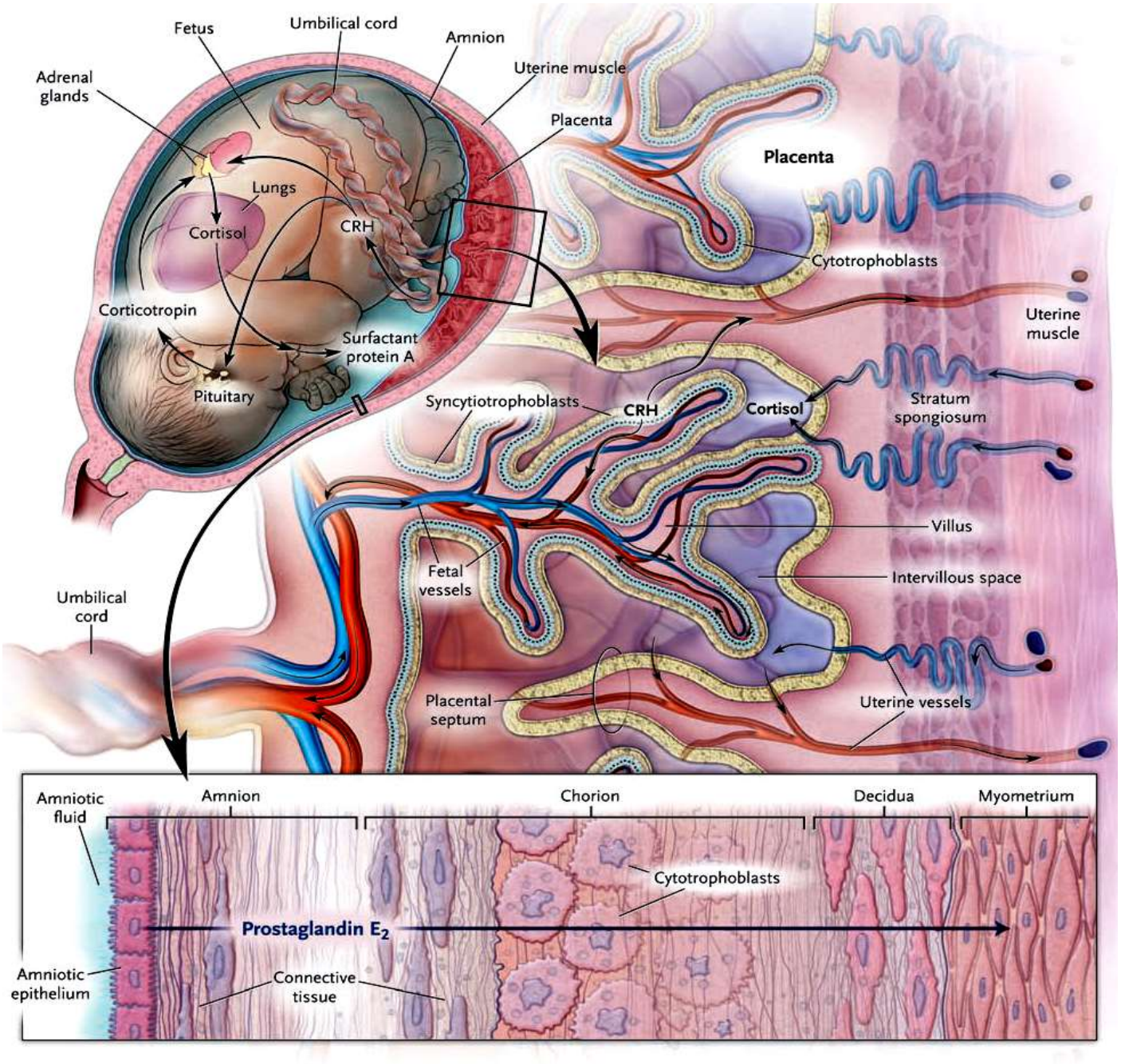

Fig. (1): Maternal–Fetal Interactions (**Smith, 2007**).

Cervical changes during prelabor and labor

The normal human cervix in the nullipara is about 2.5 cm to 3 cm in length, 2 cm to 2.5 cm in its anteroposterior diameter and 2.5 cm to 3 cm in its lateral diameter. This difference is due to the shape of the cervical canal, which is straight in the sagital plane and spindle shaped in the frontal plane. The wall of the cervix is about 1 cm thick throughout its length **(Danforth, 1983).**

During pregnancy, the length of the cervix remains relatively unchanged but it varies in width by about 1 to 2 cm. The external os usually remains firmly closed up to the 15th week of pregnancy. From the 15th to 20th week it dilates in 30% of primigravidas and in 39% of multigravida. In the subsequent course of pregnancy, the external os dilates in a further number of women **(Mclnnes et al., 1980).**

The internal os does not remain closed up to the full term pregnancy, it shows little dilatation from the 24th to the 28th week of pregnancy **(Mclnnes et al., 1980).**

The process of connective tissue remodeling in the cervix during pregnancy occurs in four stages: softening, ripening, dilation, and repair. Although overlapping in time, each stage is uniquely regulated **(Word et al., 2007).**

Although the cervix contains a small amount of smooth muscle, its major component is connective tissue. Rearrangement of this collagen-rich connective tissue is necessary to permit functions as diverse as maintenance of a pregnancy to term, dilatation to facilitate delivery, and repair following parturition so that a successful pregnancy can be repeated **(Ludmir and Sehdev, 2000).**

Throughout pregnancy, collagen is actively synthesized. It is also continuously remodeled by collagenase, secreted from both cervical cells and neutrophils in an apparently slow and precise fashion. Collagen is degraded by collagenase both intracellularly, to remove structurally defective procollagen to prevent the formation of weak structural collagen, and extracellularly, to slowly weaken (so-called softening or ripening) the collagen matrix to allow delivery of the pregnancy**(Phyllis and Leppert., 1995)**.

As gestation advances, degradation and extraction of collagen from cervical tissue (a phenomenon not observed in non-pregnant state), by collagenase (now called matrix metalloproteinases) helps to maintain balance between newly synthesized collagen thus regulating total collagen concentration in the cervix **(Phyllis and Leppert., 1995).**

Cervical changes During Labor:

Dilatation and effacement of the cervix during labor are not only a result of uterine contraction, but are also dependent upon ripening processes within the cervix **(Nuutila et al., 1999).**

The laboring cervix is histologically marked by the presence of neutrophils, and they account for a further significant increase in the level of protease found in the cervix and serum **(Osmers et al., 1992).**

Word et al., (2007), indicated that cervical ripening precedes myometrial contractions of labor by several weeks as evidenced by serial measurement of cervical length and this suggests that parturition in women is a process of long duration and that uterine contraction of labor are late events in parturition process.

Before the onset of labor the cervix become softer which facilitate dilation of the cervix once forceful myomtrial contraction of labor begin.