PRIMROSE OIL AND PRE-INDUCTION CERVICAL RIPENING

"RANDOMISED DOUBLE BLIND CONTROLLED TRIAL"

Thesis
Submitted for partial fulfillment of the Master Degree
In Obstetrics and Gynecology

By

Manal Elsayed Ahmed Hefny
B.B.Ch., (١٩٨٩) Zagazig University
Specialist of Obstetrics and Gynaecology
Kafr Sakr Urban Center , kafr Sakr, Sharkia , Egypt

Under Supervision Of

Prof. Maher Abd Elrazak Omran

Professor of Obstetrics and Gynecology

Faculty of Medicine – Ain Shams University

Dr. Ahmed Adel Tharwat

Lecturer in Obstetrics and Gynecology

Faculty of Medicine – Ain Shams University

Faculty of Medicine
Ain Shams University
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List of Abbreviations

AP : A/nteroposterior
ARM : Artificial Rupture of Membranes
cAMP : Cyclic Adenosine Monophosphate
CL : Cervical Length
CMs : Certified Midwives
CNMs : Certified Nurse-Midwives
COX-١ : Cyclooxygenase-١
CRH : Corticotrophin-Releasing Hormone
C S : caesarean section
CTG : Cardiotocography
DGLA : Dihomo - Gamma-Linolenic Acid
DNA : deoxyribonucleic acid
DSHEA : Dietary Supplement Health and Education Act
DSPG : Dermatan Sulphate Proteoglycan
EASI : Extra - amniotic Saline Infusion
ECM : Extracellular Matrix
EFAs : Essential Fatty Acids
EPO : Evening Primrose Oil
FDA : Food and Drug Administration
FHR : Fetal Heart Rate
GAGs : Glycosaminoglycans
G B S : Group B Strep
GE : Glandular Epithelium
GLA : Gamma-Linolenic Acid
GRAS : Generally Recognized As Safe
HA : Hyaluronic Acid
hCG : Human Chorionic Gonadotrophin

IOL : Induction Of Labor

IUFD : Intrauterine Fetal Death

IUGR : Intrauterine Growth Restriction

LA : Linoleic Acid

LMP : Last Menstrual Period

L-NAME : Nitro-L-Arginine Methyl Ester

LOA : Left Occipito-Anterior

LSCS : Lower Segment Caesarean Section

LUS : Lower Uterine Segment

MCP : Monocyte Chemotactic Protein

MMP : Matrix Metalloprotein

m-RNA : messenger RNA

NO : Nitric Oxide

NOS : Nitric Oxide Synthease

NRFHT : Non Reassuring Fetal Heart Test

NMR : Nuclear magnetic resonance

PE : Pre-Eclampsia

PET : Pre-Eclamptic Toxaemia

PGE_1 : Prostaglandin E_1

PGE_2 : Prostaglandin E_2

PGL : Proteoglycan

PGs : Prostaglandins

PGHS : Prostaglandin endoperoxide H Synthetase

PIH : Pregnancy-Induced Hypertension

PMS : Premenstrual Syndrome

PPROM : Preterm Prelabor Rupture Of the Membranes

PROM : Prelabor Rupture Of Membranes

RCTs : Randomized Controlled Trials

RCOG : Royal Collage of Obstetricians and Gynaecologists

RNA : Ribo Nucleic Acid

SEM **:** Scanning Electron Microscopy

SGA **:** Small-for-Gestation-Age

SM **:** Smooth muscle

SVD : Spontanuous Vaginal Deliveru

TAGs : Triacylglycerol

TIMPs **:** Tissue Inhibitors of Matrix metalloproteinases

TLR **:** Toll – Like Receptor

TNF **:** Tumour necrosing factor

TVU **:** Transvaginal Ultrasound

TXA٢ **:** Thromboxane

VEGF **:** Vascular Endothelial Growth Factor

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دراسة عشوائية محكمة مزدوجة التعمية

رسالة

توطئة للحصول على درجة الماجستير

فى أمراض **النساء والتوليد**

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الأستاذ الدكتور/ ما هر عبد الرزاق عمران

أستاذ أمراض النساء والتوليد

كلية الطب- جامعة عين شمس

الدكتور/ احمد عادل ثروت

مدرس أمراض النساء والتوليد

كلية الطب- جامعة عين شمس

كلية الطب

جامعة عين شمس

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Faculty of Medicine

Ain Shams University

INTRODUCATION

Induction of labor refers to the iatrogenic stimulation of uterine contractions before the onset of spontaneous labor to accomplish vaginal delivery ***(Gabbe et al., ٢٠٠٧)***.

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 weighted 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. For the last ٢ decades, the rate of labor induction in the United States has more than doubled, with more than ٢٢٪ of all pregnant women in ٢٠٠٦ having labor induced. This increase in use necessitates a careful review of indications, risks, and benefits ***(Barclay ,*** ***d***). In ٢٠٠٤ and ٢٠٠٥, one in every five deliveries in the United Kingdom was induced ***(NICE Guide Line ٧٠,*** ***.***).

Throughout history, obstetric providers have used various techniques to induce labor, many of which are not formally documented or included in induction statistics. Some of these techniques include mechanical measures e.g.,(membrane stripping, extra-amniotic balloon catheter, hygroscopic cervical dilators, artificial rupture of membranes, or digital stretching),

pharmaceutical e.g., prostaglandin analogs, oxytocin, relaxin, or mifepristone , and “natural” techniques e.g: castor oil, enemas, sexual intercourse, evening primrose oil, nipple stimulation, acupuncture, acupressure, or homeopathy ***(Declercq et al . , ٢٠٠٦).***

Non-pharmacological methods of induction should be explored for use at health center level for non urgent and elective inductions as they are inexpensive, require little monitoring and have been shown through systematic reviews to pose little risk to mother and baby **(*Lovod &Stanton.,* .).**

Cervical ripening is a process that occurs prior to labor in which the cervix is softened, thinned, and dilated. It is the culmination of several biochemical changes that result in a physically soft cervix. During the complex ripening process, collagen fibers of the cervix break down as the water content of the cervix increases. The process results in a reduction in cervical resistance ***(James et al., ٢٠٠٦).***

The success of induction and labor progression is dependent on the condition of the cervix before induction initiation. To assess cervical readiness for labor, or its “ripeness,” a cervical exam is performed to determine specific evaluative criteria. The cervix is given a Bishop score, which indicates predictive readiness for labor using five factors . A bishop score of ٦ or more indicates

an increased readiness for effective labor. An induction that starts with a Bishop score of ٨ or more has the same chance of a vaginal birth for labor that began spontaneously. When the score is unfavorable (<٥) , prostaglandin analog treatment and alternative therapies are considered to facilitate the process of cervical ripening before the onset of labor According to both the WHO (***WHO***) and the American College of Obstetricians and Gynecologists (***Barclay .,***).

In primigravidae , the mean time taken from induction to delivery is between ١٥ and ٢٠ hours, of which up to ١٢ hours is spent in the cervical ripening phase before labor itself starts. There is increasing interest in carrying out cervical ripening on an outpatient basis ***(Stitely et al.,*** ***)***.

An agent that ripened the cervix without stimulating uterine activity would be the ideal cervical ripening agent for outpatient use ***(Thomson et al., ١٩٩٧, Thomson et al.,*** ***) .***

According to a ١٩٩٩ national survey of herbal preparations prescribed by certified midwives (CMs) or certified nurse-midwives (CNMs) to stimulate labor, a number of oils and herbs are commonly used, including castor oil, blue and black cohosh, evening primrose oil, and red raspberry leaf**.** Although evening primrose oil is the remedy most commonly used by

midwives, it is unclear whether this substance can ripen the cervix or induce labor (***Mc Farlin et al.,*** ***).***

Evening Primrose Oil (*Oenothera biennis*) is extracted from the seed of the evening primrose plant and it is a dietary supplement that contains essential fatty acids (omega-٣ a nd o mega-٦) and has been investigated in-depth for its effectiveness for conditions that are associated with a deficiency in essential fatty acids. It is added to foods as a source of essential fatty acids and used in topical products such as soaps and cosmetics (***Blumenthal ,*** ***).***

Evening Primrose Oil (EPO) contains the amino acid tryptophan and an unusually high content of essential fatty acids, especially cis-linoleicacid (CLA) and gamma-linoleic acid (GLA). These are prostaglandin precursors which may explain anecdotal reports of the herb's apparent effectiveness in stimulating cervical ripening as well as in preventing heart disease and obesity **.**It has been widely studied in Europe and is licensed in the United Kingdom for treating atopic eczema, mastalgia, PMS, psoriasis, multiple sclerosis, hypercholesterolemia, rheumatoid arthritis, Reynaud's disease, Sjo¨gren's syndrome, chronic fatigue syndrome, asthma, diabetic neuropathy, and alcoholism .It is recommended as a dietary supplement in pregnancy as a natural source of essential fatty acids and has been documented to increase the total fat

content of breast milk ***(Blumenthal , ١٩٩٧).***

Side effects associated with the ingestion of EPO are rare at recommended dosages and include mild gastrointestinal effects and headache. *Martindale: The ExtraPharmacopoeia* (***Reynold , ١٩٩٦)*** lists caution in using this herb in patients with a history of epilepsy, as temporal lobe epilepsy can be induced and diagnosed by using EPO**.** Care must be taken when prescribing EPO to patients on antidepressants, phenothiazines , and epileptogenic drugs ***(Varga and Veale , ١٩٩٧)***.