

Isosorbide Mononitrate versus Prostaglandins for Pre-induction of Labor at Term Pregnancy

Thesis

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بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

قالوا

سبحانك لا علم لنا
إلا ما علمتنا إنك أنت
العليم العظيم

صدق الله العظيم

سورة البقرة الآية: ٣٢



وَأَنْزَلَ اللَّهُ عَلَيْكَ
الْكِتَابَ وَالْحِكْمَةَ
وَعَلَّمَكَ مَا لَمْ تَكُنْ
تَعْلَمُ وَكَانَ فَضْلُ
اللَّهِ عَلَيْكَ عَظِيمًا

صدق الله العظيم

سورة النساء الآية (١١٣)

بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

(... رَبِّ أَوْزِعْنِي أَنْ أَشْكُرَ نِعْمَتَكَ

الَّتِي أَنْعَمْتَ عَلَيَّ وَعَلَى وَالِدَيَّ

وَأَنْ أَعْمَلَ صَالِحًا تَرْضَاهُ

وَأَدْخِلْنِي بِرَحْمَتِكَ

فِي عِبَادِكَ الصَّالِحِينَ)

صدق الله العظيم

النمل.. آية رقم ١٩



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and The Most Merciful.*

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List of Abbreviations

<i>Abbrev.</i>	<i>Full term</i>
APH	: Antepartum hemorrhage
AROM	: Artificial rupture of membrane
bNOS	: Brain nitric oxide synthase
C.S	: Cesarean section
cGMP	: Cyclic guanosine monophosphate
COX-2	: Cyclooxygenase-2
CRF	: Corticotropin releasing factor
CTG	: Cardiotocography
ECM	: Extracellular matrix
EDC	: Estimated date of confinement
eNOS	: Endothelial nitric oxide synthase
FHR	: Fetal heart rate
GAGs	: Glycosaminoglycans
GTN	: Glyceryl trinitrate
IL8	: Interleukin 8
IMN	: Isosorbide mononitrate
iNOS	: Inducible nitric oxide synthase
ISMP	: Institute for safe medication practices
LMP	: Last menstrual period

List of Abbreviations

<i>Abbrev.</i>	<i>Full term</i>
LPS	: Lipopolysaccharides
Mcg - µg	: Microgram
MIU	: Mill international unit
MMP	: Matrix metaloprotienase
nNOS	: Neuronal nitric oxide sysnthase
NO	: Nitric oxide
NOS	: Nitric oxide sysnthase
PAF	: Platelet activating factor
PGDH	: Prostaglandin dehydrogenase
PGE2	: Prostaglandin E2
PPROM	: Premature preterm rupture of membrane
TNF	: Tumer necrosis factor
U/S	: Ultrasound scanning

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Introduction

The continuation of a woman's pregnancy requires that her cervix remains closed and rigid and that her uterus quiet and not contracting. Both these conditions need to be reversed to initiate labour. The ways in which this is achieved are unknown but there is evidence that suggests the fetus itself plays an integral part. A woman's cervix, which contains little smooth muscle and is predominantly connective tissue with collagen as its main component, must undergo a process called ripening, where it becomes soft and pliable. This allows its shape to change from being long and closed to being thinned (effaced) and opening (dilating) (*The Information Centre CHS, 2006*).

Induction of labour is a common intervention in obstetric practice. In the Western world, labour is induced in one of every four pregnant women for reasons related to increasing risks for the mother, for example, hypertension, pre-eclampsia, diabetes or increasing risks for the fetus such as suspected fetal growth retardation. Moreover the rate of elective inductions i.e. induction without a medical indication, is rising rapidly. Reasons for wanting elective induction at term might include a woman's physical discomfort, convenience of providers, or concern about the rapid progression of labour away from the hospital. Some clinicians may recommend elective induction due to concern about future complications (*Boulvain, 2008*).

Artificial cervical ripening is a component part of induction of labor that is used when the cervix is unfavorable to facilitate cervical dilation when labor is established. Because the success of induction is related to cervical ripening, artificial cervical ripening before labor induction is used to reduce the associated risk of cesarean delivery (*Osman et al., 2006*).

Induction of labor (IOL) in the presence of an unripe cervix is associated with failed induction, failure to progress in labor, and an increased risk of chorioamnionitis and cesarean section (CS) (*Furukan et al., 2007*).

The goal of labour induction is to achieve a successful vaginal delivery, although induction exposes women to a higher risk of a CS than spontaneous labour. Before induction, there are several clinical elements that need to be considered to estimate the success of induction and minimize the risk of CS. Factors that have been shown to influence success rates of induction include the Bishop score, parity (prior vaginal delivery), BMI, maternal age, estimated fetal weight, and diabetes (*Gülmezoglu et al., 2006*).

In ancient times women and medical workers already tried to influence the natural course of labor and provoke contractions by using herbs, tonics and other remedies; Hippocrates described mammary stimulation and mechanical dilatation of the cervical canal as a method to stimulate labor

through the 18th century, mechanical methods to induce labor came into use.

In 1756, at a meeting held in London, physicians discussed the efficacy and ethics of early delivery by rupturing the membranes to induce labor. In 1810, James was the first in the United States to utilize amniotomy to induce preterm labor.

Amniotomy and other mechanical methods like laminaria or inflating balloons remained the most commonly employed methods of labor induction until the 20th century (*ACOG, 2009*).

The drugs commonly used in hospital settings, such as prostaglandins E2 (PGE2, dinoprostone) and prostaglandin E1 (PGE1, misoprostol), are effective for cervical ripening. However, the high incidence rates of myometrial hyperstimulation, uterine hypertonus, tachysystole, and fetal distress associated with their use (*Agarwal et al., 2012*).

In contrast to prostaglandins, nitric oxide donors such as isosorbide mononitrate (IMN) and glyceryl trinitrate inhibit rather than stimulate uterine contractions, and promote rather than restrict uterine blood flow. Therefore, nitric oxide donors appear to be the ideal cervical ripening agent for outpatient use (*Ekerhovd et al., 2003*).