بسم الله الرحمن الرحيم

MONA MAGHRABY

شبكة المعلومات الجامعية

التوثيق الالكتروني والميكروفيلم

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شبكة المعلومات الجامعية

التوثيق الإلكتروني والميكروفيلم

جامعة عين شمس

التوثيق الإلكتروني والميكروفيلم

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MONA MAGHRABY

A comparison of the efficacy and safety of repetitive hourly dose of oral misoprostol and two hourly dose oral regimens for cervical ripening and labor induction: A R.C.T

A Thesis

Submitted for partial fulfillment of master degree
in Obstetrics & Gynecology

By

Essam Salah Mohamed Hagag
M.B.B.Ch., Faculty of Medicine – Ain Shams University (2012)

Under Supervision of

Prof. Dr. Sabry Sayed Mohamed
Professor of Obstetrics and Gynecology
Faculty of Medicine, Ain Shams University

Dr. Hayam Fathy Mohammed
Assistant Professor of Obstetrics and Gynecology
Faculty of Medicine, Ain Shams University

Dr. Ahmed Mohammed Essam El Din Mansour
Lecturer of Obstetrics and Gynecology
Faculty of Medicine, Ain Shams University

Faculty of Medicine
Ain Shams University
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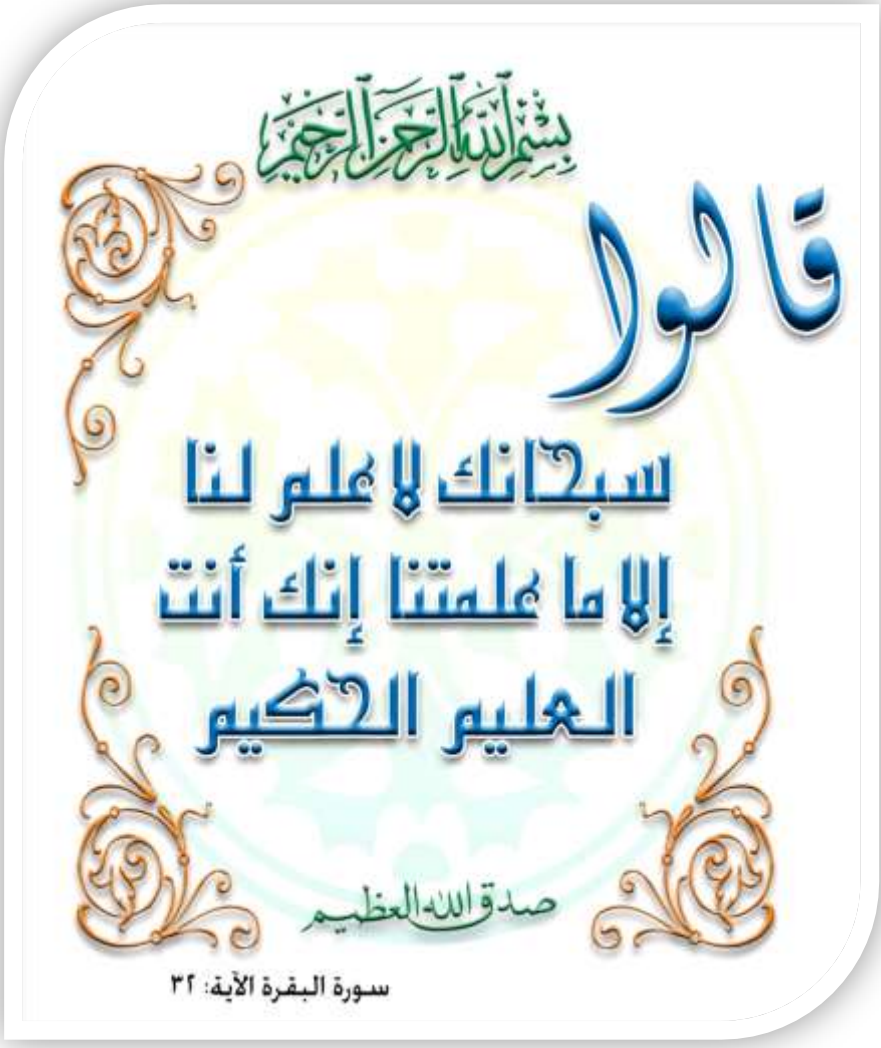
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Essam Salah Mohamed Hagag

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List of Abbreviations

Abbr.	Full-term
ACOG	**:** American College of Obstetricians and Gynecologists
BMI	**:** Body mass index
CI	**:** Confidence interval
FDA	**:** Food and Drug Administration
FHR	**:** Fetal heart rate
GBS	**:** Group B Streptococcus
HELLP	**:** Hemolysis, elevated liver enzymes, low platelets
HR	**:** Hazard ratio
IOL	**:** Induction of labor
IV	**:** Intravenous
NO	**:** Nitric oxide
NSAIDs	**:** Non-steroidal anti-inflammatory drugs
OR	**:** Odds ratio
PG	**:** Prostaglandin
RR	**:** Relative risk
SPSS	**:** Statistical package for social science
UK	**:** United Kingdom

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Introduction

Induction of labor (IOL) is defined as artificial stimulation of uterine contractions before the spontaneous onset of labor, with or without ruptured membranes, Labor induction most frequently conducted through interventional procedures, and their use has been increasing in the past several decades. In a survey by the National Center for Health Statistics the rate of labor induction was noted to have increased from 9.5% in 1991 to 22.5% in 2006 ***(Chung et al., 2015).***

Methods for induction of labor can be mechanical or pharmacological. Mechanical means of labor induction include the use of various types of catheters and hygroscopic dilators introduced into the cervical canal or into the extra-amniotic space. Pharmacological methods include prostaglandins, mifepristone and oxytocin ***(Hofmeyr et al., 2010).***

Two types of prostaglandin preparations, natural prostaglandin E2 (dinoprostone) and synthetic prostaglandin E1 (misoprostol), are currently approved by the US Food and Drug Administration for pre-induction cervical ripening. Dinoprostone although widely used, has two disadvantages: it is expensive and requires continuous refrigeration ***(Asunción et al., 2017).***

Misoprostol, therefore, which is less expensive and more stable at room temperature, has been proposed as an alternative agent for labor induction. However, misoprostol may lead to adverse effects such as gastrointestinal disturbance, uterine tachysystole, and the most severe, uterine rupture ***(Thaisomboon et al., 2012).*** These adverse effects are likely to be dose and route related ***(León et al., 2012).***

The more frequent dosing may address the short half-life of misoprostol, which is reported to reach the highest serum peak concentration (300-800 pg./mL) in approximately 14-30 minutes, with a terminal half-life of 20- 40 minutes ***(Abdul Rahim et al., 2017).***

Induction regimens using vaginal misoprostol have raised concerns of hyper stimulation and fetal heart rate changes due to the longer half-life and direct effect of misoprostol on the cervix.

The presence of vaginal secretions, bleeding, or leaking amniotic fluid can contribute to inconsistent dose absorption, concentration, and variable peak plasma levels when misoprostol is administered vaginally ***(Weeks et al., 2007).***

Additionally, dosing may be difficult to determine secondary to broken pill fragments when breaking 200 mcg pills into 25 mcg doses for vaginal administration. Overall, oral administration of misoprostol has a rapid onset with

consistent doses that are not affected by the presence of vaginal bleeding or discharge; and decreased risk of infection from ascending bacteria by preventing multiple sterile vaginal examinations.

In addition to the route of administration and dosage, it is also apparent that the duration and the time interval between doses play an important role in the efficacy and safety of oral misoprostol for cervical ripening and labor induction ***(Morris et al., 2017).***

Induction of labor is commonly performed in hospital settings using a range of interventions. In recent years there has been increased interest in the use of outpatient induction of labor. In this setting, women attend the hospital to receive the induction agent and then return home afterwards. They then return to the hospital when they start to contract regularly, or if they require further interventions.

Induction of labor in an outpatient setting is therefore, restricted to low-risk circumstances when cervical ripening and labor induction is carried out without an ongoing requirement for continuous or frequent maternal or fetal monitoring. The use of outpatient induction of labor attempts to balance potential improvement in maternal satisfaction, convenience, reduced length of hospitalization and lower cost, with safety of both mother and fetus ***(Adelson et al., 2013).***

A study by Cheng et al. showed that oral misoprostol for labor induction was associated with a lower incidence of uterine hyper stimulation and a lower cesarean delivery rate in patients with an unfavorable cervix; however, this study compared oral and vaginal routes of misoprostol administration ***(Cheng et al., 2008).***