



شبكة المعلومات الجامعية
التوثيق الإلكتروني والميكرو فيلم

بسم الله الرحمن الرحيم



MONA MAGHRABY



شبكة المعلومات الجامعية
التوثيق الإلكتروني والميكروفيلم



شبكة المعلومات الجامعية التوثيق الإلكتروني والميكروفيلم



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التوثيق الإلكتروني والميكروفيلم

جامعة عين شمس

التوثيق الإلكتروني والميكروفيلم

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MONA MAGHRABY

**Vaginal progesterone 400 mg v.s 200 mg
for prevention of preterm labor in
twin pregnancies: a randomised
controlled trial**

A Thesis

**Submitted for Partial Fulfillment of Master Degree
In Obstetrics & Gynaecology**

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بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

قالوا

سبحانك لا علم لنا
إلا ما علمتنا إنك أنت
العليم العليم

صدق الله العظيم

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List of Abbreviations

<i>Abbr.</i>	<i>Full-term</i>
ACOG	: American College of Obstetricians and Gynecologists
ART	: Assisted reproductive technology
BMI	: Body mass index
BPP	: Biophysical profile
BV	: Bacterial vaginosis
BVAB1	: BV-associated bacterium 1
CRH	: Corticotropin-releasing hormone
GBS	: Group B streptococci
NST	: Nonstress test
PAMG-1	: Placental alpha-microglobulin-1
pIGFBP-1	: Phosphorylated insulin-like growth factor binding protein-1
PPROM	: Preterm premature rupture of membranes
PTBS	: Preterm births
PTL	: preterm labor
PUPPP	: Pruritic urticarial papules and plaques of pregnancy
SD	: Standard deviation
sFGR	: Selective fetal growth restriction
sFlt-1	: Soluble fms-like tyrosine kinase-1
SPSS	: Statistical package for social science
sPTB	: Spontaneous PTB
TAPS	: Twin anemia-polycythemia sequence
TTTS	: Twin-twin transfusion syndrome
TVU	: Transvaginal ultrasound

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Abstract

Abstract

Objectives: To compare between the effectiveness and safety of two different daily doses of vaginal progesterone (400 vs. 200 mg) in the prevention of preterm labor in twin pregnancy.

Methods: This is a prospective single-blinded randomized controlled trial conducted on 100 primi-gravida who had twin pregnancy and attended the antenatal clinic of a University hospital. They were equally and randomly allocated into two arms each containing 50 patients. Arm 1 received 400 mg and arm 2 received 200 mg vaginal progesterone daily at bed time starting from 14 weeks of pregnancy to 36 weeks. Transvaginal ultrasound was performed for assessment of the length of cervix at 14 and 22 weeks.

Results: Both arms of the current study were comparable regarding the cervical length at 14 and 22 weeks, mean gestational age at delivery, incidence of pre-term delivery, birth weight of the first twin. Second twin in addition to the average weight of both twins. No statistical significance differences between two arms regarding incidence of early neonatal death. NICU, mechanical ventilation, length of admission in NICU for the first twin. Second twin as well as both twins.

Conclusions: Vaginal progesterone treatment with different doses was tolerable, but wasn't effective in the prevention of preterm labor in twin pregnancy.

Keywords: cervical length; prematurity; preterm birth; progesterone; twin; vaginal progesterone.

Introduction

Twin pregnancy is associated with higher rates of almost every potential complication of pregnancy, with the exceptions of postterm pregnancy and macrosomia. The most serious risk is preterm delivery, which plays a major role in the increased perinatal mortality and short-term and long-term morbidity observed in these infants. Higher rates of fetal growth restriction and congenital anomalies also contribute to adverse outcome in twin births. In addition, monochorionic twins are at risk for complications unique to these pregnancies, such as twin-twin transfusion syndrome (TTTS), which can be lethal or associated with serious morbidity (*Chasen et al., 2020*).

Preterm birth (PTB) refers to a delivery that occurs between 20 and 37 weeks of gestation (a delivery before 20 weeks is a miscarriage in the United States, although the upper gestational age threshold for miscarriage varies worldwide). It may or may not be preceded by preterm labor. Seventy to eighty percent of PTBs are spontaneous: due to preterm labor (40 to 50 percent) or preterm premature rupture of membranes (20 to 30 percent); rarely cervical insufficiency results in spontaneous PTB. The remaining 20 to 30 percent of PTBS are iatrogenic: due to maternal or fetal issues that jeopardize the health of the mother or fetus (eg,

preeclampsia, placenta previa, abruptio placenta, fetal growth restriction, multiple gestation). Complications of pregnancy can lead to both spontaneous and provider-initiated PTBs (**Robinson et al., 2019**).

PTB is relatively common, occurring in 5 to 18 percent of births worldwide. There are many risk factors for PTB and many pathways from these risk factors to the terminal cascade of events resulting in labor. Preterm labor likely occurs when local uterine factors prematurely stimulate this cascade or suppressive factors that inhibit the cascade and maintain uterine quiescence are withdrawn prematurely. The four major factors leading to preterm labor are intrauterine infection, decidual hemorrhage, excessive uterine stretch, and maternal or fetal stress. Uteroplacental vascular insufficiency, exaggerated inflammatory response, hormonal factors, cervical insufficiency, and genetic predisposition also play a role (**Robinson et al., 2019**).

Ideally, identification of modifiable and nonmodifiable risk factors for PTB before conception or early in pregnancy will lead to interventions that help prevent this complication. However, few interventions have been proven to prolong pregnancy in women at risk. This goal has been elusive for several reasons: two-thirds of PTBs occur among women with no risk factors, causality has been difficult to prove (eg,

a cofactor may be required thus complicating the chain of causality), and no adequate animal model exists for study of spontaneous PTB (sPTB) (**Robinson et al., 2019**).

Multifetal gestation accounts for only 2 to 3 percent of all births but 17 percent of births before 37 weeks of gestation and 23 percent of births before 32 weeks. The widespread availability of assisted reproductive technology has resulted in a large increase in the incidence of multiple gestations; this increase, in turn, has led to an increase in spontaneous and indicated PTB. The mechanism for sPTB in multifetal gestations, and particularly higher-order multifetal gestations, may be related to sequelae of increased uterine distension. The endocrine environment produced by superovulation or the multiple pregnancy may also play a role. As an example, multifetal gestations produce increased amounts of estrogen, progesterone, and sex steroids compared with singleton pregnancies. Increased steroid production may be a factor in initiation of labor. Higher circulating levels of relaxin associated with super-ovulation may cause cervical insufficiency with subsequent sPTB (**Kiely, 2017**).

Prevention and reduction of multifetal gestations, particularly high-order multifetal gestations, appear to improve neonatal outcome. In unselected twin pregnancies,

progesterone supplementation, use of a pessary, cerclage, and bed rest/reduction of physical activity do not prolong gestation (**Kiely, 2017**).

Although supplemental progesterone appears to be effective in preventing preterm birth in some high-risk women, it should not be seen as a panacea. Even if all pregnant women in the United States with a history of preterm birth receive progesterone prophylaxis, it is estimated that the risk of preterm birth would be reduced by 20 percent and the absolute preterm birth rate would be reduced by only 0.01 percent because most preterm births are not recurrences and prophylaxis has limited efficacy. If women with a short cervix are also identified and treated, an additional absolute risk reduction of 0.02 percent would be achieved. (**Norman and Bennett, 2017**).