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Original article

Effect of Vaginal Progesterone after Tocolytic Therapy in Threatened Preterm Labour

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Abstract:

Background: Preterm labor, accounts for the vast majority of infant mortality and morbidity. One of perinatal care primary goals is now the prevention of preterm labor. **Aim:** to determine whether vaginal progesterone maintenance medication could lengthen the latency period following a successful episode of preterm labor, this study examined this possibility. **Methods:** The women were split into two groups when the uterine contractions stopped: 50 patients made up the first group (the study group). A micronized vaginal progesterone supplement was administered to women daily in doses of 200 mg. Progesterone vaginal suppository was continued, and the women were told to reduce their physical activity, until 36 weeks of gestation. There were 50 patients in the second group (the control group). In addition to being told to minimize their physical activity, women were not offered any medicines or follow-up care. Patients were kept in the hospital if labor pain persisted; otherwise, if they were stable, they were released**. Results:** the study discovered that vaginal progesterone lower the risk of labor before 37 weeks of gestation for women who are more likely to high risk for preterm labor. Accordingly, treatment with progesterone agents to lessen preterm birth complications should continue to women who are at risk. **Conclusion:** In this study, it was discovered that preventive treatment of 200 mg vaginal suppositories of progesterone following successful tocolysis was linked to a longer gestation period and improved fetal outcomes in high-risk patients.

Key Words: preterm; vaginal labor, progesterone.

Introduction

The phrase "preterm birth" refers to births that occur before 37th week of pregnancy (between 20 and 37 weeks), when there are uterine contractions that are frequent and efficient enough to cause the cervix to gradually dilate and be effaced. Nearly 50% of preterm births were preceded by premature labor, and preterm birth, which affects 12% of pregnancies and is the main cause of newborn mortality in the US [(1)].

Preterm birth rates typically range from 5 to 9 percent in Europe and many other affluent nations; in the USA, they have even increased to 12 to 13 percent over the past few decades [(2)].

It is still unclear what causes labor, and it is also unclear what causes preterm birth. Labor is a complicated process that incorporates many different elements: intrauterine inflammation or infection, premature fetal endocrine activation, uterine overdistension and decidual hemorrhage- are the four different pathways that could result in premature delivery [(3)].

Other causes may contribute to preterm labor: stress, placental abruption, placenta previa, substance use, history of preterm birth or abortion, inadequate prenatal care, smoking, maternal age <18 or >40, poor nutrition, low body mass index, fetal anomaly, fetal growth restriction, oligohydramnios, polyhydramnios, vaginal bleeding, premature preterm rupture of membranes (PPROM), and environmental factors [(4,5)].

Progesterone clearly plays a role in the maintenance of pregnancy, there is evidence that progesterone reduces the likelihood of premature birth. Progesterone levels are maintained until the end of pregnancy and in labor, but complex alterations in progesterone receptor activity result in a decline in progesterone receptor signaling at the time of labor onset [(6,7)].

Aim of the work: The work's purpose is to determine whether vaginal progesterone maintenance medication following a successfully treated episode of preterm labor could lengthen the latency period.

Subjects and Method:

One hundred pregnant women who were at high risk for preterm delivery after the termination of a previous episode of preterm regular uterine contractions participated in this prospective, randomized trial, at Benha university hospital, from May 2023 till December 2023 .

The study was done after approval of the Research Ethical Committee of Benha faculty of medicine with the code RC27-5-2023.

Inclusion criteria:

Pregnancy in a Singleton.

Pregnancy age of 28–36 weeks determined from the first day of the LMP regular menstrual cycle and/or by ultrasound during the first trimester.

.Membrane integrity.

.No cervix cerclage.

The following criteria were used to make the diagnosis of preterm labor: regular uterine contractions happening three times in 10 minutes, together with a gradual change in the cervix, and cervical effacement of less than fifty percent. Furthermore, a 2 cm cervical dilation [(8)].

Exclusion criteria:

- Clinical proof of an intrauterine infection, vaginal hemorrhage, or pre-eclampsia.
- Fetal growth restriction as determined by ultrasound.

Fetal congenital defects.

Methods: all women : were subjected to:

Full physical examination and history taking

Obstetric ultrasound to:

.Calculate the AFI, or Amniotic Fluid Index.

.Validates the gestational age .

.Rule out multiple pregnancies

.Rule out uterine and fetus congenital abnormalities.

Steps:

- All patients received 500 cc of saline solution intravenously
- Tocolytic therapy: After administering an initial bolus of 4-6 mg of magnesium sulphate intravenously to the patients, and continued as 1 gm per hour for 24 other doses
- Antibiotics: For 48 hours, intravenous ampicillin (2 gm every 12 hours) was administered to all patients as part of an antibiotic prophylactic.
- Corticosteroids: To lower the incidence of infant respiratory distress syndrome, intraventricular hemorrhage, and perinatal death- all patients received a single course of corticosteroids, consisting of two injections of 12 mg dexamethasone, during the first 24 hours after admission.

Patients were kept in the hospital if labor pain persisted, and if they were stable, they were released. Patients were told to come back for follow-up appointments every two weeks .

Following cessation of uterine contraction, the ladies were split into two groups:

Study group

Micronized progesterone (prontogest) 200 mg vaginal suppository was given to the women every day. The women were told to reduce their physical activity and keep using progesterone vaginally suppository until 36 weeks of gestation.

Control group

Women were not offered any medicines or follow-up care. In addition to being told to minimize their physical activity, patients were instructed to return to the hospital in cases of repeated uterine contractions and to be managed in accordance with the needs of the mother and the fetus.

Outcome

The gestational age, delivery method, and perinatal outcome- were recorded as delivery specifics. Birth before 37 completed weeks of gestation- was deemed a preterm delivery. It was divided into two categories: preterm births that occurred between 34 & 37 weeks and those that occurred before 34 weeks, the latency time (the interval between admission and delivery, birth weight and perinatal morbidity and mortality.

Statistical methods

The collected data underwent revision, coding, and tabulation using the IBM SPSS Statistics software (Version 27.0, IBM Corp., Released 2019@Chicago).

P value: ≤0.05 is significant

Results

The control group had an average age of 26.2 ± 4.5 ranging from 18 to 35 years, and study group had an average age of 26.5 ± 4.7, ranging from 18 to 34 years. The study group's mean gestational age ranged from 28 to 36 weeks, whereas the control group's ranged from 30 to 36 weeks, respectively. Forty four % of the study population and 28 % of the control population- were nulliparous, while 32 % of the study population and 20 % of the control population had previously given birth (Table 1).

Table (1): Demographic data of the studied groups

Age	**Study group(n 50)**	**Control group (n = 50)**	**T**	**P**
Mean ± SD	26.5 ± 4.7	26.2 ± 4.5	0.63	0.57 (NS)
Range	18-35	18-34		
Gestational age at admission				
Mean ± SD	32 ± 1.5	32 ± 2	0.28	0.77(NS)
Range	28-36	30-36		
Parity				
Nullipara	22 (44%)	14 (28%)	2.78	0.09(NS)
Multipara	28 (56%)	36 (72%)	1.8	0.17(NS)
Positive history of preterm labor	16 (32%)	10 (20%)	1.8	0.17(NS)

The study group's latency period (7.4±4.1weeks) is longer than the control group's (3.3± 4.4 weeks) till delivery (Table 2). In the study group, the prevalence of preterm birth before 34 weeks was 16% (Table 3).

Table (2): Gestational age at delivery and latency period.

	study group (n = 50)	**control group (n = 50)**	**T**	**P**
Gestational age at delivery (weeks)				
Mean ± SD	37.6 ± 2.7	33.6 ± 4.7	4.96	< 0.001 (HS)
Range	32-40	28-36		
Latency (weeks)				
Mean ± SD	7.4 ±4.1	3.3 ±4.4	MW = 24.3	< 0.001 (HS)
Range	2-7	1-4		

MW = Mann-Whitney

Table (3): Outcome results among studied groups.

	study group (n = 50)	**control group (n = 50)**	**X^2**	**p**
Preterm birth before 34 weeks	8 (16%)	24 (48%)	11.76	< 0.001 (HS)
Preterm birth before 37 weeks	12 (24%)	34 (68%)	19.48	< 0.001 (HS)
Neonatal outcome				
Birth weight (kg)	3.75 ± 0.6	2.89 ± 0.4		0.46
Apgar < 7	4 (8%)	6 (12%)		0.5
Admission to NICU	2 (4%)	3 (6%)		1
RDS	6 (12%)	10 (20%)		0.27
Sepsis	0 (0%)	4 (8%)		0.11
Neonatal death	1 (2%)	8 (16%)		0.03

Discussion

Obstetricians' top priority is to prevent premature delivery because it is the main cause of newborn morbidity and mortality [(9)]. Preterm birth rates have increased over the past 20 years and have continued to rise, mostly as a result of the growth in multiple pregnancies brought on by assisted reproduction [(10)].

Treatment of patients displaying even the smallest symptoms of premature contraction- is a well-known problem; the therapy causes unneeded hospitalization, wastes medical staff time, and costs money [(11)].

It has been proven that progesterone reduces PTB in high-risk groups of females. Two double blind trials with weekly 17-hydroxyl progesterone intramuscular injections and daily vaginal progesterone suppositories- claimed that the therapies significantly decreased PTL [(6)].

In our study, 50 women were included in the study group, which received 200 mg of vaginal progesterone to prevent PTL, and 50 cases were considered the control group out of the 100 women who had been diagnosed with threatened PTL.

In this study, the incidence of preterm delivery before 34 weeks was 16% and that of preterm birth before 37 weeks was 24% and that of control group was 68%. Similar findings from the study of da Fonsea [(12)]. According to da Fonsea 142

women were recruited, and they took 100mg of vaginal progesterone every night from 24 to 34 weeks. They discovered a significant decrease in premature labor at 34 weeks (17% in study group, 46% in control group, and preterm birth before 37 weeks 26% in the study group and 69% in the control group 69%) [12].

A second trial used vaginal progesterone 100mg for 71 singleton pregnancies prior to PTB. Daily suppositories between (24 - 34) weeks were linked to a substantial decrease in the occurrences of PTB at (37 - 34) weeks (24% vs. 50%) and (34 - 34) weeks (5.4% vs. 26.5%) compared to the placebo group [13].

When compared to the control group in this study, the study group's latency length to delivery was longer (7.4 ± 4.1 weeks vs. 3.3 ± 4.4 weeks), with a p value of 0.001. The latency period was shown to be longer (7.3 ±4.3) than the control group (3.3 ± 4.4) in Borna's second study in 2018, which had 70 women receiving 400 mg of vaginal progesterone daily [14].

The results of this study show that administering 200mg of progesterone vaginally is efficient in preventing preterm labor contributing in prolongation of latency period allowing time for enhancing fetal lung maturity & increasing gestational birth weight so, minimizing neonatal morbidity & mortality and is more comparable to conservative measurement.

In contrast, 17-hydroxyl progesterone therapy was linked to a longer latency period and a shorter PTl, according to Monari et al. [15]. They found that the latency time in their study, which included 75 women separated into study and control groups, was (35.3 ± 19) days in the study group and (25.5± 15.1) days in the control group [15].

In his study on 657 singlet gestations between 16 and 24 weeks using 250 mg I.M. weekly, the incidence of PTL at 35 weeks was 13.5 versus 16.1% and p value, 0.03; at 37 weeks, it was 15, indicating that patients treated with 250 Mg I.M. 17 hydroxyl progesterone had better outcomes than those treated with vaginal progesterone [16].

Conclusion

This study found a relationship between a longer gestation time and better fetal outcomes when patients with threatening idiopathic PTL received preventive treatment with 200 mg vaginal progesterone suppositories after successful tocolysis.

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