

Vaginal Progesterone versus Cervical Cerclage or Both for Prevention of Preterm Delivery

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ABSTRACT

Background: Preterm labor (PTL) occurs in 5-13% of pregnancies before 37 weeks' gestation. Multiple pregnancy and iatrogenic preterm birth remain important causes of prematurity. Three interventions have been proposed to treat patients with a sonographic short cervix: (1) vaginal progesterone administration, (2) cervical cerclage for patients with a history of preterm birth and (3) vaginal pessary. **Aim of the work:** evaluate the efficacy of vaginal progesterone supplementation, cervical cerclage, or a combination of both in the prevention of PTL and their impact on the perinatal outcome. **Patients and methods:** Randomized controlled trial done on asymptomatic women with a sonographic short cervix (cervical length <25 mm) in the midtrimester, singleton gestation, and previous spontaneous preterm birth at less than 37 weeks of gestation. The study conducted in the Obstetrics and Gynecology Department at Sohag General Hospital. **Results:** this study showed that there was no significant difference between the 4 studied groups regarding each of age, cervical length and gestational age. It also showed that either vaginal progesterone only or cerclage only reduced the risk for preterm labor significantly compared to control. Moreover, combination of cerclage and vaginal progesterone resulted in higher reduction of preterm labor.

Keywords: Cervical Cerclage, Cervical Incompetence, Preterm Delivery, Vaginal Progesterone.

INTRODUCTION

Preterm labor (PTL) occurs in 5-13% of pregnancies before 37 weeks' gestation. The incidence of early PTL (<34 gestational weeks) is 1-3.6%. Preterm birth remains the leading cause of perinatal morbidity and mortality worldwide ⁽¹⁾. Multiple pregnancy and iatrogenic preterm birth remain important causes of prematurity, however, the prevention of recurrent spontaneous preterm birth in singletons has been highlighted recently by the USA Food and Drug Administration approving, and the American College of Obstetricians and Gynecologists endorsing⁽²⁾. Most of the efforts to prevent preterm birth have been focused on the treatment of symptoms or signs of activation of the common pathway of parturition^(3,4) i.e., increased uterine contractility^(5,6) preterm cervical ripening⁽⁷⁾ and/or membrane decidual activation^(8,9).

Although the detection of increased uterine contractility⁽¹⁰⁾ has been the focus of clinicians and reproductive biologists for decades, emerging clinical⁽¹¹⁾ and laboratory-based evidence⁽¹²⁾ suggests that focusing on the uterine cervix may yield approaches to identify the patient who is at risk for preterm delivery as well as interventions to prevent it^(13,14). Three interventions have been proposed to treat patients with a sonographic short cervix: (1) vaginal progesterone administration,⁽¹⁵⁾ (2) cervical cerclage for patients with a history of preterm birth⁽¹⁶⁾ and (3) vaginal

pessary⁽¹³⁾. Recently, a combination of vaginal progesterone and a pessary has been reported to be a successful method to reduce the rate of preterm delivery in twin gestations with a cervix of <25 mm⁽¹⁷⁾.

The availability of vaginal progesterone and cerclage for the prevention of preterm birth in women with a short cervix, singleton gestation, and previous spontaneous preterm birth could create a dilemma for physicians and patients about the optimal choice of treatment. Thus far, there are no randomized controlled trials comparing vaginal progesterone and cerclage directly. In the absence of this evidence, indirect meta-analysis has emerged as an accepted and valid method for the comparison of competing interventions with the use of a common comparator⁽¹⁸⁾.

AIM OF THE STUDY

To evaluate the efficacy of vaginal progesterone supplementation, cervical cerclage, or a combination of both in the prevention of PTL and their impact on the perinatal outcome.

PATIENTS AND METHODS

Study Design:

Randomized controlled trial

Subjects:

Asymptomatic women with a sonographic short cervix (cervical length <25 mm) in the midtrimester, singleton gestation, and previous

spontaneous preterm birth at less than 37 weeks of gestation.

Setting

The study was conducted in the Obstetrics and Gynecology Department at Sohag General Hospital. **The study was approved by the Ethics Board of Al-Azhar University.**

Inclusion criteria

High-risk women for PTL with singleton pregnancy and at least one prior preterm birth before 34 weeks, who were found to have a short cervical length detected on transvaginal ultrasound examination.

Exclusion criteria:

- Women with multiple gestations.
- Underweight and obese women.
- History of failed previous cerclage.
- History of high risk pregnancy.
- Women with actual or threatened preterm labor, second trimester bleeding or premature rupture of membranes.

The cases were subjected to:

- Careful history taking.
- Careful clinical examination.
- BMI to detect and exclude underweight and obese women.
- Routine laboratory investigation (Hemoglobin level, blood sugar, urine analysis, PLTs, WBCs , Coagulation profile , TSH ,.....).
- Regular blood pressure measurement.
- Ultrasonographic(US) assessment
- Notification of each studied case in individual clinical sheet.

Grouping of the cases:

The studied cases had been divided into four groups:

-Group (A): Control group (50 cases) normal pregnant cases were not received any intervention.

-Group (B): Case group (50 cases) received vaginal progesterone supplementation till maturity (detected either by expected date of delivery (EDD) and/or US assessment).

-Group (C): Case group (50 cases) were having a cervical cerclage at 12 weeks of pregnancy.

-Group (D): Case group (50 cases) had a cervical cerclage at 12 weeks of pregnancy and received vaginal progesterone supplementation till maturity (detected either by EDD and or US assessment).

Technique of cervical cerclage:

A McDonald cerclage was done. This cerclage is placed at 12 weeks of pregnancy. The stitch was generally removed around the 37th week of gestation.

Patients monitoring and Follow up:

- Careful clinical and self monitoring for early and wearing signs and symptoms of PTL.
- Gestational age when labour occurred.
- Outcome of the pregnancy of the studied cases.

Statistical analysis

All the collected data were organized, tabulated and analyzed and appropriate statistical tests were conducted on qualitative and quantitative data accordingly.

RESULTS

Table (1) show that there was no significant difference between our 4 studied groups regarding each of age, cervical length, and gestational age.

Table (2) table shows that either vaginal progesterone only or cerclage only reduced the risk for preterm labor significantly compared to control. Moreover, combination of cerclage and vaginal progesterone resulted in higher reduction of preterm labor.

Table 1. Comparison between studied groups

Variable Mean±SD	Groups				F value	P value
	Control	Vaginal progesterone only	Cerclage only	Cerclage + Vaginal progesterone		
Age	27.70±4.514	27.64±3.79	27.74±4.593	27.64±4.055	0.007	.99 (NS)
Cervical length	20.32±2.788	19.78±2.985	20.42±2.67	20.26±2.625	0.527	0.664 (NS)
Gestational age	19.74±2.940	19.74±2.940	19.74±2.940	19.74±2.940	0.000	.000 (NS)

Table (2) Outcome of pregnancy

Group		Outcome		Total
		Term delivery	Preterm delivery	
Control	No	26	24	50
	%	52.0%	48.0%	100.0%
Vaginal Progesterone only	No	34	16	50
	%	68.0%	32.0%	100.0%
Cerclage only	No	35	15	50
	%	70.0%	30.0%	100.0%
Cerclage + Vaginal Progesterone	No	40	10	50
	%	80.0%	20.0%	100.0%
Total	No	133	67	200
	%	66.5%	33.5%	100.0%

Chi square = 9.185, p value = **0.027 (S)**

DISCUSSION

Shortened cervical length, measured by transvaginal ultrasound, has emerged as a consistently powerful predictor of spontaneous preterm birth and several treatment strategies have been proposed⁽¹⁹⁾. A recently published individual patient data meta-analysis of five randomized trials provided evidence that, when compared with placebo, vaginal progesterone reduces both the preterm birth rates before 33 weeks’ gestation (relative risk (RR)=0.58; 95% CI, 0.42–0.80) and neonatal mortality/morbidity (RR=0.57; 95% CI, 0.40–0.81) when prescribed to asymptomatic pregnant women with a short cervix (≤ 25 mm)⁽²⁰⁾. These results were not replicated in a study in which 17 α -hydroxyprogesterone caproate was used in nulliparas with cervical length less than 30mm⁽²¹⁾. A Cochrane review of cerclage for preterm birth prevention in singleton pregnancy reported a less marked, but statistically significant, reduction in preterm birth when cerclage was compared with no treatment⁽²²⁾.

The reduction in preterm births after cerclage was consistent across commonly reported gestational cut-off periods (<37, <34 and <28 weeks’ gestation) and for all prespecified clinical subgroups, including ultrasound-indicated cerclage for high-risk women. The benefit of cerclage for women with singleton pregnancy, short cervix and previous preterm birth was also highlighted in the meta-analysis⁽¹⁶⁾. The aim of our study was to compare effect of cervical cerclage, vaginal progesterone or both in prevention of preterm labour and their impact on perinatal outcome.

In this study, there was no significant difference between our 4 studied groups regarding each of age, cervical length, and gestational age.

Regarding outcome, we found that either vaginal progesterone only or cerclage only reduced the risk for preterm labor significantly compared to control. Moreover, combination of cerclage and vaginal progesterone resulted in higher reduction of preterm labor. Our results were similar to study done by *Alfirevic et al.*⁽²³⁾ as their results suggested similar effectiveness of currently available treatment strategies (vaginal progesterone and cerclage) for women with singleton pregnancy who have at least one prior preterm birth and a shortened cervical length detected by transvaginal ultrasound examination.

O’Brien et al. carried out a descriptive cross sectional study over a 2 years period on patients having history of 2 or more recurrent midtrimester abortions/preterm deliveries. They reported 73.7% of term delivery after application of cervical cerclage, 18.7% of premature delivery and 7.5% of miscarriages⁽²⁴⁾. Another study⁽²⁵⁾ also demonstrated 76% of term deliveries, 12% preterm deliveries and 10% of abortions.

In another study⁽²⁶⁾ women allocated to receive vaginal progesterone had significantly lower risk of preterm birth <33 weeks’ gestation compared with those allocated to placebo/no treatment. In addition, vaginal progesterone was associated with a significant reduction in the risk of preterm birth <35 weeks’ gestation, <34 weeks’ gestation, <32 weeks’ gestation, <30

weeks' gestation (RR, 0.47 (95% CI, 0.25–0.86); moderate-quality evidence), and spontaneous preterm birth at <33 weeks' gestation and <34 weeks' gestation.

Another study⁽²⁷⁾ showed that vaginal progesterone significantly decreased the risk of preterm birth ≤34 weeks of gestation or fetal death by 34%, among women with a singleton gestation and a midtrimester cervical length (CL) ≤25 mm. Clearly, the reduction in this composite outcome is attributable to a decrease in preterm birth ≤34 weeks of gestation rather than fetal death because vaginal progesterone had no effect on the risk of this adverse outcome in the meta-analysis of data from the OPPTIMUM study⁽²⁸⁾.

CONCLUSION

This study concluded that either vaginal progesterone or cervical cerclage had a significant beneficial effect in the protection against preterm delivery among high risk women. The combination of cervical cerclage and vaginal progesterone gave higher protective effect than any method alone.

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