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Use of Progesterone to Reduce Preterm Birth

ABSTRACT: Preterm birth affects 12% of all births in the United States. Recent studies support the hypothesis that progesterone supplementation reduces preterm birth in a select group of women (ie, those with a prior spontaneous birth at <37 weeks of gestation). Despite the apparent benefits of progesterone in this high-risk population, the ideal progesterone formulation is unknown. The American College of Obstetricians and Gynecologists Committee on Obstetric Practice believes that further studies are needed to evaluate the use of progesterone in patients with other high-risk obstetric factors, such as multiple gestations, short cervical length, or positive test results for cervicovaginal fetal fibronectin. When progesterone is used, it is important to restrict its use to only women with a documented history of a previous spontaneous birth at less than 37 weeks of gestation because unresolved issues remain, such as optimal route of drug delivery and long-term safety of the drug.

Preterm birth affects 12% of all births in the United States. This statistic has led multiple investigators to identify those women at greatest risk (eg, those with prior preterm delivery, maternal weight <50 kg, African-American race, bleeding, and concurrent sexually transmitted diseases). Despite identification of these risk factors, no interventions to date have been associated with a decrease in preterm delivery rates.

A recent large randomized placebo-controlled trial comparing 17α hydroxyprogesterone caproate "17P" therapy to prevent preterm birth in a select, high-risk group of women (documented history of a previous spontaneous preterm birth <37 weeks of gestation) was conducted for the National Institute of Child Health and Human Development (NICHD) Maternal-Fetal Medicine Units Network (1). A total of 459 women with a history of previous spontaneous births at less than 37 weeks of gestation were enrolled between 16 weeks and 20 weeks of gestation. Of note, the mean gestational age of their previous preterm deliveries was 30.7 weeks. They were randomly assigned to receive weekly intramuscular injections of 17P (n = 306) or placebo (n = 153). The study was stopped early when results showed a significant protection against recurrent preterm birth for all races of women who received 17P (Table 1).

A recent small randomized placebo-controlled trial of supplemental vaginal progesterone (100 mg daily) in 142 women at high risk for preterm birth

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Table 1. Rates of Preterm Labor with Progesterone Therapy or Placebo

Gestation	Placebo Group (n = 153)	Progesterone Group (n = 306)	Relative Risk	Confidence Interval	*P*
<37 wk	54.9%	36.3%	0.66	0.54–0.81	.0001
<35 wk	30.7%	20.6%	0.67	0.48–0.93	.0165
<32 wk	19.6%	11.4%	0.58	0.37–0.91	.0180

Data from Meis PJ, Klebanoff M, Thom E, Dombrowski MP, Sibai B, Moawad AH, et al. Prevention of recurrent preterm delivery by 17 alpha-hydroxyprogesterone caproate. N Engl J Med 2003;348:2379–85.

(women with at least 1 previous spontaneous preterm birth, prophylactic cervical cerclage, and uterine malformation) revealed that for delivery at less than 34 weeks of gestation, the preterm birth rate was significantly lower among women receiving progesterone than among those receiving placebo (2.7% versus 18.6%) (2). The results of this study and the NICHD trial support the hypothesis that progesterone supplementation reduces preterm birth in a select very high-risk group of women.

Despite the apparent benefits of progesterone in a high-risk population, the ideal progesterone formulation is unknown. The 17P used in the NICHD trial was specially formulated for research and is not currently commercially available on a wide scale. Progesterone has been studied only as a prophylactic measure in asymptomatic women, not as a tocolytic agent. Whether vaginal progesterone is equally efficacious remains to be proved in a larger population. The American College of Obstetricians and Gynecologists Committee on Obstetric Practice believes that further studies are needed to evaluate the use of progesterone in patients with other high-risk obstetric factors, such as multiple gestations, short cervical length, or positive test results for cervicovaginal fetal fibronectin. When progesterone is used, it is important to restrict its use to only women with a documented history of a previous spontaneous birth at less than 37 weeks of gestation because unresolved issues remain, such as optimal route of drug delivery and long-term safety of the drug.

References

1. Meis PJ, Klebanoff M, Thom E, Dombrowski MP, Sibai B, Moawad AH, et al. Prevention of recurrent preterm delivery by 17 alpha-hydroxyprogesterone caproate. N Engl J Med 2003;348:2379–85.
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