Risk of Preterm Birth with Vaginal Progesterone in Twin Pregnancies

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This series is coordinated by John E. Delzell Jr., MD, MSPH, Assistant Medical Editor.

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Clinical Question

Does vaginal progesterone in twin pregnancies reduce the risk of preterm birth?

Evidence-Based Answer

Women with twin pregnancies should not routinely receive vaginal progesterone because it does not reduce the risk of preterm birth. (Strength of Recommendation [SOR]: A, based on a systematic review of high-quality randomized controlled trials [RCTs].) Vaginal progesterone should be administered to reduce adverse neonatal outcomes in women with twin pregnancies and a short cervix (25 mm or less). (SOR: B, based on a subgroup analysis of systematic reviews of high-quality RCTs and an additional RCT.) The use of vaginal progesterone probably reduces the risk of preterm birth before 34 weeks' gestation in dichorionic twin pregnancies in women with a short cervix. (SOR: C, based on a single RCT.)

Evidence Summary

A 2014 systematic review and meta-analysis included seven RCTs of women with twin pregnancies from 16 weeks' to 23 weeks, 6 days' gestation (N = 1,731).[1] Patients were randomized to receive 90 to 400 mg of vaginal progesterone per day vs. placebo or no treatment, and were followed through delivery and neonatal discharge. There was no significant difference in the composite adverse perinatal outcome (perinatal death, respiratory distress syndrome, intraventricular hemorrhage, and necrotizing enterocolitis) or preterm birth before 37, 35, 32, or 28 weeks' gestation. A subgroup analysis of women with a short cervix found a significant reduction in the composite adverse perinatal outcome (five trials; N = 116; relative risk [RR] = 0.57; 95% confidence interval [CI], 0.47 to 0.70; number needed to treat [NNT] = 10).

A 2012 systematic review and meta-analysis included five RCTs of pregnant women with a short cervix in the second trimester who received vaginal progesterone (90 to 200 mg daily) vs. placebo or no treatment for the prevention of preterm birth (N = 775, with subgroup analysis of 52 twin pregnancies from three trials).[2] These trials were included in the 2014 meta-analysis discussed previously, but the outcomes differed. Patients were followed through delivery, then for 18 to 24 months. Vaginal progesterone did not significantly reduce preterm birth before 33 weeks' gestation (RR = 0.70; 95% CI, 0.34 to 1.44). There was a significant reduction in composite neonatal morbidity and mortality (perinatal death, respiratory distress syndrome, intraventricular hemorrhage, necrotizing enterocolitis, and neonatal sepsis) in women who received vaginal progesterone (RR = 0.52; 95% CI, 0.29 to 0.93). Conclusions were limited by the small subgroup size.

A 2016 RCT of women 20 to 35 years of age with a dichorionic twin pregnancy and cervical length of 20 to 25 mm compared vaginal progesterone (400 mg daily) vs. no treatment for the reduction of preterm birth (N = 322).[3] Follow-up occurred every two weeks throughout delivery and the neonatal period. Treatment reduced the risk of preterm birth before 34 weeks' gestation (RR = 0.67; 95% CI, 0.49 to 0.91; NNT = 6), birth weight less than 1,500 g (3 lb, 5 oz; RR = 0.46; 95% CI, 0.30 to 0.71; NNT = 8),

respiratory distress syndrome (RR = 0.68; 95% CI, 0.55 to 0.84; NNT = 6), need for mechanical ventilation (RR = 0.47; 95% CI, 0.33 to 0.69; NNT = 6), and early neonatal death (RR = 0.49; 95% CI, 0.33 to 0.73; NNT = 7).

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Author disclosure: No relevant financial affiliations.

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