Studies Back Progesterone to Prevent Preterm Birth

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SAN FRANCISCO — Recent studies provide some guidance in applying recommendations from the American College of Obstetricians and Gynecologists on the use of progesterone to prevent preterm birth, Steve Caritis, M.D., said at a meeting on antepartum and intrapartum management, sponsored by the University of California, San Francisco.

Only intramuscular injections of 17-hydroxyprogesterone caproate (17-OHPC) have been shown convincingly to prevent recurrent preterm birth, he said.

The American College of Obstetricians and Gynecologists in 2003 recommended that progesterone may be used to help prevent preterm birth but should be restricted to pregnant women with a documented history of spontaneous preterm birth before 37 weeks' gestation. The statement noted that "the ideal progesterone formulation remains unknown until further research is done."

A 1990 metaanalysis of studies using 17-OHPC found that this agent dramatically lowered the risks for preterm labor and preterm birth.

Although some individual studies had shown a benefit, most were too small to detect significant changes in benefit. When combined in the metaanalysis, they provided the power to show a dramatic impact of 17-OHPC, which reduced the overall odds of preterm labor by 43%, and the odds of preterm birth in women at high risk for preterm birth by 50%, he said.

A separate study conducted for the National Institutes of Child Health and Human Development Maternal-Fetal Medicine Units Network randomized 459 pregnant women who had at least one previous preterm birth to receive weekly injections of 17-OHPC or placebo starting between gestational weeks 16 and 20. The study was stopped early when it became evident that 17-OHPC decreased the risk for preterm birth before 37 weeks by 34%.

Critics of that study noted that the control group had a very high rate of preterm birth and that castor oil (in which 17-OHPC is dissolved) is a uterine stimulant., said Dr. Caritis, who is professor and chief of maternal-fetal medicine at the University of Pittsburgh.

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Both the treatment and control groups received castor oil, so it is hard to argue that this created a methodologic problem, he added. The preterm birth rate among controls was similar, however, to rates seen in two other studies and was not unexpected, he said.

Critics also noted a higher rate of spontaneous abortions at less than 20 weeks in the 17-OHPC group. The five spontaneous abortions in that group were counted as preterm births, so there would have been a more significant benefit in the 17-OHPC group, compared with placebo, if these losses had been excluded, he countered.

"I think this is still the best study we have" on preventing preterm birth with progesterones, Dr. Caritis said.

A third study randomized 142 women with singleton gestations and a history of preterm birth to vaginal suppositories of 100 mg of progesterone or placebo starting at 24-34 weeks' gestation, later than the 16-20 weeks' initiation in the 17-OHPC trial.

Results showed a 50% reduction in preterm birth before 37 weeks of gestation with the progesterone suppositories and an 85% reduction in preterm births before 34 weeks' gestation. The latter result "makes me a little suspicious," he said.

The vaginal suppository trial excluded patients with preterm premature rupture of the membranes (PPROM). "We don't think that's appropriate. It's hard to differentiate preterm labor with or without PPROM," Dr. Caritis said. His institution offers only 17-OHPC to women with previous spontaneous preterm birth. For now, they do not give this treatment to women who have a short cervix, threatened preterm labor, or multifetal gestation.

Studies are underway in the maternal-fetal medicine units network evaluating 17-OHPC treatment for those indications. ■