Antiangiogenic State May Be Key in Preeclampsia

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MIAMI BEACH — Serum levels of soluble endoglin and soluble fms-like tyrosine kinase 1 are increased months before onset of clinical disease in patients with preeclampsia, Dr. Richard Levine said at the annual meeting of the Society for Maternal-Fetal Medicine.

The findings suggest that a circulating antiangiogenic state is important in the pathogenesis of this maternal syndrome, said Dr. Levine of the National Institute of Child Health and Human Development, Bethesda, Md.

"We believe that soluble endoglin [a cell surface receptor for the proangiogenic protein transforming growth factor–β] and soluble fms-like tyrosine kinase 1 [an antiangiogenic factor that binds placental growth factor and vascular endothelial growth factor] act in concert to produce the maternal syndrome of preeclampsia," he said.

A nested case-control study of the Calcium for Preeclampsia Prevention (CPEP) trial cohort of healthy nulliparas showed that compared with serum samples from gestational age–matched controls, the levels of these factors were significantly higher beginning 9-11 weeks before preterm preeclampsia. After preeclampsia onset, soluble endoglin (sEng) levels were almost fivefold higher (46 vs. 10 ng/mL) and soluble fms-like tyrosine kinase 1 (sFlt1) levels were nearly threefold higher (6,356 vs. 2,316 pg/mL). Placental growth factor (PlGF) levels were approximately fourfold lower (144 vs. 546 pg/mL), Dr. Levine said.

The findings were based on an analysis of 867 serum samples obtained from 120 controls; 120 patients with term preeclampsia; 72 patients with preterm preeclampsia; 9 patients with hemolysis, elevated liver enzymes, and low platelet count (HELLP) syndrome; and 8 patients with eclampsia. In patients with term preeclampsia, sEng was increased beginning at 12-14 weeks, free PlGF decreased beginning at 9-11 weeks, and sFlt1 increased less than 5 weeks before preeclampsia onset. Alterations in angiogenic factors were more pronounced in early preeclampsia patients and in patients with preeclampsia plus a small-for-gestational age fetus, HELLP syndrome, or eclampsia, he noted.

Laboratory studies have suggested independent roles for both sEng and sFlt1 in the development of preeclampsia. The present study was designed to test the hypothesis that in preeclampsia, excess soluble endoglin is released from the placenta into the circulation and that it may then synergize with sFlt1, which binds PlGF and vascular endothelial growth factor to cause endothelial dysfunction, he explained. Women in this analysis with high levels of either sEng or sFlt1—but not both—had small elevations in preeclampsia risk. ■

Late Progesterone Also Cuts Repeat Preterm Births

MIAMI BEACH — Progesterone prevents recurrent preterm delivery to the same degree whether it is initiated earlier or later in the second trimester, according to a poster presentation at the annual meeting of the Society for Maternal-Fetal Medicine.

"We were thinking that those who started earlier would have some benefit. But essentially it doesn't matter if you start progesterone at 16-18 weeks or between 19 and 21 weeks," said Dr. Gretchen Koontz of the ob.gyn. department at Wake Forest University in Winston-Salem, N.C.

In a 2003 study, researchers randomized women with a history of previous spontaneous preterm birth (before 37 weeks) to weekly injections of either 17 α-hydroxyprogesterone caproate (17P) or placebo (N. Engl. J. Med. 2003;348:2379-85). Of the 306 women who received 17P between 16 and 21 weeks' gestation, 36% delivered before 37 weeks, compared with 55% of the 153 women in the placebo group, a statistically significant difference.

As a secondary analysis of the original study data, Dr. Koontz compared 227 women who began weekly injections of 17P between 16 and 18 weeks, with 272 others who began 17P between weeks 19 and 21. Results showed that 36.5% of participants in the 16- to 18-week group delivered preterm, compared with 36.1% of those in the 19- to 21-week group.

—Damian McNamara