Therapy May Cut Preterm Delivery from Preeclampsia

Preeclampsia during pregnancy can lead to serious health consequences for mother and baby, but preventive and therapeutic interventions have largely been unsuccessful, in part due to a limited understanding of the pathogenesis of the condition. In fact, the only way to cure preeclampsia is to deliver the baby. Recently, however, researchers proposed one of the first therapeutic interventions for preeclampsia that could help avoid preterm delivery. The results were published in the Journal of the American Society of Nephrology.

“Based on recent advances in the understanding of this condition, we and others are developing treatments for preeclampsia to allow women to safely prolong their pregnancy if they are suffering from very preterm preeclampsia,” said lead author Ravi Thadhani, MD, MPH, Chief of Massachusetts General Hospital’s Division of Nephrology. “Prolonging pregnancy allows the baby to mature, markedly reducing complications.”

Dr. Thadhani is part of a collaborative team of scientists and clinicians from the United States and Germany that designed an open pilot study based on the knowledge that soluble FMS-like tyrosine kinase-1 (sFlt-1), which alters blood vessel growth, likely plays a role in the maternal signs and symptoms of preeclampsia. sFlt-1 binds and reduces free circulating levels of proangiogenic factors, thereby blocking their beneficial effects on the maternal endothelium.

The investigators evaluated the safety and effectiveness of removing sFlt-1 from the blood of 11 pregnant women with very preterm preeclampsia (23–32 weeks’ gestation) through apheresis, which involves passing the patient’s blood through a column lined with a material that binds to sFlt-1. sFlt-1 is retained while the rest of the blood is then returned to the body.

The 11 women received a total of 17 apheresis treatments (6 were treated once, 4 were treated twice, and 1 was treated 3 times). All participants experienced a reduction of sFlt-1, from an average pre-apheresis sFlt-1 concentration of 17,394 pg/mL to an average post-apheresis concentration of 14,265 pg/mL. The average percent reduction per treatment was 18% (range 7% to 28%) with concomitant reductions of 44% in protein/creatinine ratios. In addition to reducing proteinuria, apheresis transiently reduced women’s blood pressure.

Pregnancy continued an average of 8 days for women treated once and 15 days for women treated multiple times. Pregnancy continued for only 3 days in 22 untreated women with preeclampsia. No major adverse effects of apheresis were observed as compared with infants born prematurely to untreated women with and without preeclampsia. Also, newborn babies of women in the apheresis group required fewer days of supplemental oxygen compared with those born to women in the preeclampsia control group, which suggests less pulmonary pathology.

“Our pilot study suggested we can safely prolong pregnancy when we target removal of sFlt-1 in women with severe preterm preeclampsia, and we hope this is confirmed in randomized trials,” said Dr. Thadhani.

In an accompanying editorial, Thomas Easterling, MD, of the Maternal and Infant Care Clinic at the University of Washington Medical Center, in Seattle, noted that apheresis may be an important component of a broader intervention of synergistic agents, but he questioned whether the observed reduction in sFlt-1 concentration is clinically significant.

“Achieving an additional week of gestational age in a premature infant at the gestational ages studied is important and, given the cost of care in the neonatal intensive care unit, probably cost-effective,” he wrote. He noted that approximately 20,000 women per year, 0.5%
of 4 million births in the United States, develop preeclampsia before 34 weeks gestation. Dr. Easterling agreed with the study’s authors that a randomized trial is needed, but designing and carrying one out will be challenging.

Other experts in the field also welcomed the results and look forward to additional research on the strategy. “The study by Thadhani et al. is fascinating. As a physician scientist working in this field, I am thrilled to see this study whereby a molecule that is pathologically linked to preeclampsia and associated with adverse outcomes was used to identify a patient population for directed therapy but was also used to monitor response to therapy,” said Santhosh Rana, MD, Section Chief of Maternal Fetal Medicine at the University of Chicago. “This is science at its very best, and I am happy that it is happening to benefit our pregnant moms and their babies.”

Study co-authors include Henning Hagmann, MD, Wiebke Schaarschmidt, MD, Bernhard Roth, MD, Tuey Cinogez, MD, S. Ananth Karumanchi, MD, Julia Wenger, MPH, Kathrynn Lucchesi, PhD, RPh, Hector Tamez, MD, MPH, Tom Lindner, MD, Alexander Fridman, MD, Ulrich Thome, MD, Angela Kribs, MD, Marco Danner, Stefanie Hamacher, MSc, Peter Mallmann, MD, Holger Stepan, MD, and Thomas Benzing, MD.

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The article, entitled “Removal of sFlt-1 by Dextran Sulfate Apheresis in Preeclampsia,” is available at http://jasn.asnjournals.org/.


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