Researchers identify key contributor to pre-eclampsia

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A new study by researchers at Wake Forest University School of Medicine reveals a key component in the development of preeclampsia in pregnant women, a condition that can result in miscarriage and maternal death.

The study, funded by the National Institutes of Health, appears in the September issue of *Endocrinology*.

In it, researchers focused on identifying the differences in the uteri of pregnant women with and without preeclampsia and how the mother's tissues vary from the immediately adjacent fetus' tissue in preeclamptic women.

"Preeclampsia is a very serious condition that affects 7 to 10 percent of all pregnancies in the United States," said K. Bridget Brosnihan, Ph.D., the lead investigator for the study and a professor in the Hypertension and Vascular Research Center at the School of Medicine. "It can be devastating to both mother and baby, and currently there is no cure except to deliver the fetus. Our finding brings us one step closer to understanding the condition by getting a picture of what is happening at the maternal and fetal interface."

Preeclampsia is a disorder that occurs only during pregnancy and the postpartum period. It is a rapidly progressive condition that impacts multiple body systems, causing high blood pressure, decreased liver function and, in the most severe cases, affecting the activity of the brain,

resulting in seizures. Swelling, sudden weight gain, headaches and changes in vision are among the symptoms; however, some women with rapidly advancing disease report few symptoms.

Left untreated, preeclampsia can lead to serious, even fatal, complications for both mother and baby. The condition contributes significantly to neonatal morbidity and mortality and is the second leading cause of maternal death. By conservative estimates, preeclampsia and other hypertensive disorders during pregnancy are responsible for 76,000 maternal and 500,000 infant deaths each year, according to the Preeclampsia Foundation.

Despite numerous research studies, the specific causes of preeclampsia remain a mystery. One possible pathway that has been identified is the renin-angiotensin system (RAS), which regulates blood pressure and fluid retention.

The RAS, when operating normally, forms a hormone called angiotensin II, a potent vasoconstrictor that binds to angiotensin II receptors throughout the body, including in the maternal uterine "bed" and the fetal placenta, and causes the muscular walls of blood vessels to contract, narrowing the diameter of the vessels and increasing blood pressure.

In normal pregnancy, the uterus has lower RAS activity, producing less angiotensin II, which results in the blood vessels remaining dilated. This results in lower blood pressure and allows more oxygen and nutrients to pass from the mother's uterus to the placenta and fetus, which is beneficial for its development.

In preeclamptic women, however, the activity of the RAS is increased in the uterus, yet the mother's vessels remain dilated and the fetus' vessels constrict more than normal. Brosnihan and colleagues focused on uncovering the reason for this in the current study.

What they found was surprising, Brosnihan said. Research showed that the angiotensin II receptors are not detectable in the uteri of pregnant or preeclamptic women. In normal pregnancy, this does not present a problem because there is less angiotensin II being produced, making the receptors less important. In preeclamptic women, however, where uterine angiotensin II is high, the hormone does not bind to its receptors in the uterus as it should, but instead passes through to the vessels of the fetal placenta and constricts the fetus' vessels, limiting the fetus' oxygen and nutrient intake and often causing low birth weight.

The only known way to cure preeclampsia is delivery of the baby. Women diagnosed with preeclampsia too early in their pregnancy for delivery to be an option need to allow the baby more time to mature, without putting themselves or their babies at risk of serious complications.

"The placenta is really thought to be a key cause of preeclampsia," Brosnihan said. "That's why we were interested in the interface between the mother's uterus and the fetal placenta. The placenta itself is a key factor in getting rid of the disease. Once the fetus and placenta are delivered, preeclampsia goes away, so the disease seems to originate there."

Inhibitors of the RAS are known to have bad effects on the fetus, so controlling the system is difficult in preeclamptic women, Brosnihan said. Because of its role in blood pressure regulation, many people with hypertension take medicines that work by affecting the RAS function. Those medicines, however, are contraindicated in pregnant women.

"It is very hard to control parts of this system to prevent preeclampsia without hurting the baby," Brosnihan said. "Our study provides some insight into maternal factors that may augment the disease. Hopefully, one day, we will be closer to finding a cure."

Source: Wake Forest University Baptist Medical Center (news : web)