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New findings may help explain some major clinical symptoms of preeclampsia

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Virginia Commonwealth University School of Medicine researchers have found that a significant increase of an enzyme in the blood vessels of pregnant women with preeclampsia may explain some of the symptoms associated with the condition, including hypertension, swelling and protein in the urine.

The findings could lead to a treatment for pregnant women with preeclampsia, which is one of the most significant health problems in pregnancy and a leading cause worldwide of both premature delivery and of sickness and death of the mother and baby.

Preeclampsia, a condition which occurs in one out of 20 pregnancies, is diagnosed when the mother develops high blood pressure and starts losing protein in her urine after 20 weeks of pregnancy. Research has shown that the blood vessels of women with preeclampsia are dysfunctional, but the cause of preeclampsia is not known, and the only treatment is delivery of the baby.

In a study published in the January issue of The American Journal of Pathology, the VCU team reported a significant increase in an enzyme called MMP-1 in blood vessels of women with preeclampsia and an imbalance in collagen-regulating genes that favored the breakdown of collagen. MMP-1 is an enzyme produced in tissues under conditions of inflammation that acts to break down collagen.

"The increase in MMP-1 that we found would compromise the integrity

of the mother's blood vessels, which could explain two of the clinical symptoms of preeclampsia – edema and proteinuria," said corresponding author Scott Walsh, Ph.D., professor in the VCU Department of Obstetrics and Gynecology.

The swelling experienced by pregnant women with preeclampsia is due to edema, which is a leakage of protein out of the blood vessels into surrounding tissues. Proteinuria is a leakage of protein through the blood vessels of the kidney and into the urine.

The team also found that MMP-1 causes blood vessel contraction by activation of a receptor known as PAR1, which according to Walsh, could explain the hypertension, or high blood pressure, of women with preeclampsia.

"This finding may be especially important for preeclampsia because we found increased amounts of PAR1 in blood vessels of preeclamptic women as compared to normal pregnant women. MMP-1 activation of PAR1 is a totally new mechanism to explain hypertension," Walsh said.

PAR1 is best known for its role in the coagulation of blood, but it is not known for a role in hypertension, said Walsh.

Further, the team showed that neutrophils, or white blood cells, and neutrophil products increase MMP-1 and PAR1. According to Walsh, neutrophil infiltration may be the cause of the increase in MMP-1 and PAR1 in blood vessels that leads to vessel dysfunction and clinical symptoms of preeclampsia.

"Activation of the PAR1 receptor by MMP-1 causes changes in the endothelial cells of blood vessels that we speculated could result in contraction of blood vessels. This new information provides a rationale for the use of PAR1 inhibitors to treat preeclampsia," said Walsh.

Provided by Virginia Commonwealth University