Is preeclampsia a risk or a protective factor in retinopathy of prematurity?

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Mary Elizabeth Hartnett, MD, and colleagues at the John A. Moran Center and Department of Pediatrics at the University of Utah and Children's Hospital of Wisconsin, were looking for a way to tease apart the effects of preeclampsia on the risk of developing retinopathy of prematurity (ROP), an eye disease found in premature infants. Their results, and the model they developed, were published February 14, 2017, in *Scientific Reports*.

In ROP, blood vessels in the retina grow outside of their normal space. This can lead to blindness. In addition, there is a strong link to premature birth—the more premature the infant, the more likely the infant is to develop ROP and the more severe the ROP may be. Previous research has also found an association between premature birth and preeclampsia. The linkage between premature birth and ROP, and between premature birth and preeclampsia, makes it difficult to tease apart the effect of preeclampsia on risk for ROP.

Preeclampsia is a high blood pressure condition in pregnant women that can lead to decreased blood flow to the placenta. Hence, both preeclampsia and ROP are linked to premature birth, and reports in the literature indicate either increased risk or apparent protective effects of preeclampsia on ROP. Therefore, researchers asked what the association between preeclampsia and ROP would be in the absence of premature birth.

In this report, researchers reduced blood flow to the placenta in some of

the pregnant rats to create a condition called uteroplacental insufficiency (UPI), which is present in maternal preeclampsia. Other pregnant rats, the controls, underwent a sham procedure that did not cause UPI. UPI in the mother rats caused the offspring to have poor growth. All pregnant rats delivered full-term pups. Pups born to the mother rats with UPI and those born to the controls were exposed to variable oxygen, simulating a premature infant at risk for ROP.

Researchers then looked to see if the restricted blood flow caused by preeclampsia and changes in oxygen levels had any effect on weight gain or development of abnormal retinal blood vessel growth.

They anticipated that the pups born to mother rats with UPI would have more severe retinopathy. However, they found the opposite—these pups had less severe retinopathy and more normal retinal vascular development than pups born to control mother rats and placed into varying oxygen levels. The pups with less severe retinopathy also gained the same amount of weight compared to control pups in variable oxygen. Therefore, while they expected to see examples of retinopathy representative of more severe ROP, researchers found that the combination of preeclampsia and oxygen fluctuations actually reduced features of ROP in the retina.

Researchers also looked at whether growth factors needed for retina development came from the mother or if they were produced by the pups. Growth factor levels were the same in preeclampsia and control female rats and did not align with levels in pups. But the pups from the preeclampsia mothers produced greater amounts of certain growth factors, particularly erythropoietin.

These findings support the idea that those pups that are strong enough to survive induced preeclampsia may be stressed enough to induce growth factors necessary to increase normal retinal blood vessel development

and reduce ROP severity.

"This model removes premature birth—which is highly linked to preeclampsia in mothers and to ROP in premature infants—from the equation and allows us to see the effect of preeclampsia on ROP," Hartnett explained. "The impact actually is that the oxygen fluctuations in the growth-restricted pups that survive lead to a growth advantage and reduced retinopathy.

Further research is needed to determine if growth factors transferred from the mother to the fetus affect retinal development in models without induced preeclampsia and to identify levels of circulating growth factors in premature infants to refine ROP treatment.

More information: Protective effect of maternal uteroplacental insufficiency on oxygen-induced retinopathy in offspring: removing bias of premature birth. Silke Becker, Haibo Wang, Baifeng Yu, Randy Brown, Xiaokun Han, Robert H. Lane, and M. Elizabeth Hartnett. *Scientific Reports*, February 14, 2017.

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