Effect of Uric Acid on the Expressions of Vascular Endothelial Growth factor (VEGF) and sFlt-1 of Human Trophoblast Cells : Possible Implication for the Development of Preeclampsia

Division of Nephrology, Ewha Women's University, College of Medicine, Seoul, Korea

EY Park · ES Yu · YS Lee · MY Kim · SJ Kim · GB Choi · KI Yoon · DH Kang

Background : Preeclampsia is one of the most serious and common complications of pregnancy with high maternal and fetal mortality. An increased uric acid is the most sensitive marker to predict the development of preeclampsia and is often elevated before any other clinical manifestations. Since hyperuricemia in animal models and humans is associated with many of the features of preeclampsia including hypertension, vasoconstriction, proteinuria, ischemic nephropathy and vascular remodeling, we hypothesized that uric acid may play a causal role for the development of preeclampsia and/or aggravates it. Central dogma in the development of preeclampsia is defective trophoblast invasion and placental ischemia, and recently the altered expression of VEGF and sFlt-1 in placental tissue was reported as a key factor for the development of preeclampsia.

Methods and Results : In order to investigate the role of uric acid (UA) on preeclampsia and its possible mechanism related to placental angiogenesis, we performed an experiment with human trophoblast cells (JAR cells). RT-PCR, Western blotting and ELISA were performed determine to VEGF, sFlt-1 and ERK expression. UA (6-9 mg/dL) significantly down-regulated the expression of VEGF mRNA whereas UA up-regulated sFlt-1 mRNA expression by RT-PCR and protein release by ELISA. These changes in VEGF and sFlt-1 were more prominent in hypoxic condition compared to normoxia, suggesting placental ischemia can be a factor to affect the effect of UA on placental development. UA increased ERK phosphorylation in JAR cells from as early as 5 minutes of stimulation. UA-indcued increase in sFlt-1 expression was significantly blocked by the pretreatment with probencid (0.1 mM) and PD98059 (10 mM), ERK inhibitor.

Conclusion : UA may play a contributory role in the development of preeclampsia by altering the expression of VEGF and sFlt-1 in trophoblasts. This study provides the first experimental evidences to address a longstanding relationship between UA and preeclampsia. Further studies are necessary to elucidate the mechanisms involved and to evaluate the potential therapeutic possibility of UA-lowering therapy in patients with preeclampsia.