P-IS-104  Soluble fms-like tyrosine kinase 1 (sFlt-1), free VEGF and PIGF in normal pregnancy and preeclampsia

Department of Obstetrics and Gynaecology, Faculty of Medicine, Oita University, Japan
Jun Yoshimatsu, Harunobu Matsumoto, Masako Shimano, Kyomi Goto, Yasushi Kawano, Isao Miyakawa

[Objective] Placental ischemia derives unknown factors which induces systemic endothelial dysfunction in preeclampsia. Soluble fms-like tyrosine kinase 1 (sFlt-1) is an antagonist of VEGF which is produced excessively under hypoxia by trophoblastic cells. sFlt-1 could be a candidate of this unknown factor. We investigated the gestational change of sFlt-1 and free VEGF in maternal sera of normal pregnancy. We also compared the levels of sFlt-1 and VEGF between normal pregnancy and preeclampsia. [Methods] We were offered 450 sera samples from 210 normal pregnant women and 20 women with severe preeclampsia. Determination of sFlt-1 and VEGF concentration in the serum was performed with ELISA. [Results] The serum levels of sFlt-1 was low in the first trimester and decreased in the second trimester (846.2 ± 332.4 pg/ml vs. 557.1 ± 311.3 pg/ml, p < 0.001). The sFlt-1 levels in preeclampsia was significantly higher than in normal pregnancy (1,648.8 ± 678.0 pg/ml vs. 5,919.8 ± 735.6 pg/ml, p < 0.0001). In normal pregnancy, a vascular re-modeling, which causes the rise of oxygen tension in an intervillous space, is completed until 20 weeks of gestation. We speculate that the decline of sFlt-1 in the second trimester could be a reflection of the rise of an oxygen tension in an intervillous space. Hypoxic placenta in preeclampsia excessively produced sFlt-1, which provoked endothelial dysfunction.

P-IS-105  Soluble fms-like tyrosine kinase 1 (sFlt-1) production in villous trophoblast with hypoxic stimulation.

Department of Obstetrics and Gynaecology, Faculty of Medicine, Oita University, Japan
Harunobu Matsumoto, Jun Yoshimatsu, Masako Shimano, Kyomi Goto, Yasushi Kawano, Isao Miyakawa

[Objective] Placental ischemia leads to placental production of certain factors that cause maternal endothelial dysfunction in preeclampsia sFlt-1 is a circulating VEGF receptor which is able to bind VEGF at high affinity but unable to signal since the tyrosin kinase is defected. We investigated if the hypoxic villous tissue could produce higher levels of sFlt-1. [Methods] Ten normal pregnant women voluntarily provide the villous tissue of 6–9 gestational weeks. Villous tissue was incubated for 12 hours in a humidified atmosphere composed of 5% CO2 and 95% air, or 1% O2. After the incubation, sFlt-1 levels in the supernatant were measured by ELISA. Also, total RNA was extracted from the tissue and northern blotting analysis was performed. [Results] In the supernatant that exposed to hypoxia, the concentration of sFlt-1 was 20,101.6 ± 417.0 pg/ml/mg protein, which was significantly higher than that in those exposed to normoxia (11,452.1 ± 791.1 pg/ml/mg–protein, p < 0.001). Northern blotting analysis confirmed the results of ELISA. [Conclusion] In the current study, villous explant stimulated with hypoxia showed the increase of sFlt-1. Preeclampsia give rise to relatively hypoxic trophoblast tissue as a result of an impaired vascular re-modeling. sFlt-1, which acts antagonistically to VEGF could be a candidate of the substance which derived by hypoxic placenta in preeclampsia.

P-IS-106  Calcium supplementation for the prevention of Preeclampsia in low calcium intake women: A RCT

Government Medical College Nagpur, India & Reproductive Health and Research Division World Health Organization GENEVA, Switzerland
Manorama Purwar OBGYGMCH, NAGPUR and RHR Division WHO GENEVA

Background: Preeclampsia (PE) and Eclampsia (ECL) is second leading cause of maternal and Perinatal mortality and morbidity. Etiology of PE is still elusive and no cure is available today except early delivery. Methods: In multicenter randomized placebo controlled clinical trial 8325 healthy nulliparous women attending antenatal clinic before 20 week’s gestation from seven developing countries were randomized to receive either 1500 mg of oral elemental calcium (n = 4157) per day or an identical placebo (n = 4168) until delivery. Outcome measure was development of PE diagnosed as BP140/90 mmHg recorded on two occasions four hours apart with Proteinuria of 2+ on dipstick. Results: Study groups were similar at randomization with respect to several clinical and demographic variables. Loss to follow up was 3.57%. Treatment compliance was similar in both group (84.5%Vs 86.25%). Incidence of PE was lower in Ca group than in placebo group 3.8%Vs 4.2% (RR = 0.90 ; 95%CI 0.73-1.11) same is true for Preterm delivery (PTD) 9.6% Vs 10.3% (RR = 0.85 ; 95%CI 0.82-1.06). Perinatal and maternal mortality was lower in Ca group compared to placebo group. Conclusion: Calcium supplementation has a moderate protective effect on risk of PE and PTD with 30% reduction in neonatal mortality. Implications: Prenatal calcium supplementation may be a cost effective intervention to reduce the adverse outcome in maternal and perinatal health.