86. A Study on the Prediction of Toxemia by Measuring Serum Autoimmune Antibodies (SAAs) and Serum Complements

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We already reported the relationship between SAAs and the development of toxemia. This time we examined the change of SAAs and serum complements throughout pregnancy, and then studied the utility of them in predicting the occurrence of toxemia. The results are as follows;

1) Positive rates of SAAs were significantly high in toxemic group throughout whole pregnancy.

2) Statistical data of SAAs in relation to toxemia are as follows;

sensitivity75% specificity 85%
positive predictive value 57%
negative predictive value 93%

3) None of C_3c, C_4, and CH50 were found to increase or decrease markedly in both the 1st and 2nd trimester in toxemic group, suggesting no clinical significance of serum complements measurement for predicting the development of toxemia.

Therefore we thought that the measurement of SAAs were useful for prediction of toxemia.

87. The Change of Scavenger Activities against Free Radicals in Maternal Erythrocytes during Normal Pregnancy and Pregnancy Induced Hypertension (PIH)

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Activities of 2 scavenger enzymes in maternal erythrocytes against free radicals (FR), namely superoxide dismutase (SOD) and glutathion peroxidase (GSH-PX), and thiobarbituric acid reacting substances (TBARS), a sensitive indicator of lipidperoxides, in maternal plasma were investigated in the peripheral blood obtained from 70 women with normal pregnancies and 29 patients with pregnancy induced hypertension (PIH), 11 of whom were complicated intrauterine growth retardation (IUGR). During normal pregnancy, SOD activities gradually elevated with the advance of gestation, reacting 9.4 U/mg. Hb in the 3rd trimester of pregnancy. The activity markedly increased to 18.1 U in the PIH cases complicated with IUGR ($p<0.001$), and significantly lowered to 4.6 U in PIH cases without IUGR ($p<0.001$). While GSH-PX activity showed no significant change during normal pregnancy, the activity lowered significantly in the PIH cases without IUGR ($p<0.005$). TBARS in maternal plasmas were significantly high in PIH cases complicated with IUGR ($p<0.005$).

The present data clearly revealed that production of FR, possibly from the fetoplacental tissues, elevated substantially in the PIH cases complicated with IUGR, whereas the scavenger activities lowered in the PIH cases without IUGR.

FR and lipidperoxide, generated by FR, may participate in the pathogenesis of PIH, at least in respect to the changes in hemostasis characteristic to PIH, since FR and lipidperoxide could injure vascular endothelium and stimulate circulating platelets.

88. C1-inhibitor Activity in Normal Pregnancy and Preeclampsia

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C1-inhibitor is a protease inhibitor of complement C1, kallikrein, coagulation factors XII and XI, and plasmin. Recently abnormality of blood coagulation has been reported to be involved in pathophysiology of preeclampsia. In this study we measured activity of C1-inhibitor in order to find roles of C1-inhibitor during pregnancy. Plasma sample was collected from 60 pregnant women and 9 preeclamptic patients. Activity of C1-inhibitor was determined by measurement of remained C1-esterase after mixing exess C1-esterase and a sample. Activity of C1-inhibitor was 100 ± 15% (mean ± standard deviation) in early pregnancy (10~19w), 82 ± 22% in mid pregnancy (20~29w) and 84 ± 10% in late pregnancy (30w~). Negative correlation between activity of C1-inhibitor and weeks of pregnancy was significant ($p<0.01$). Antigen of C1-inhibitor showed similar decrease to its activity during normal pregnancy. Correlation between activity and antigen of C1-inhibitor is also significant. Antigen of C1q, C3 and C4 showed no significant change during normal pregnancy. Activity of C1-inhibitor in 6 preeclamptic patients with hypertension was 82 ± 19%. Three of these patients showed activity below 70%. Activity of C1-inhibitor in preeclampsia with only edema or proteinuria was 99

± 11%. Because of no change of complements, C1-inhibitor may be effective in the kinin-kallikrein system or blood coagulation.

89. Pregnancy Zone Protein and Haptoglobin Level in Gestosis

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Sera of pregnant women with or without gestosis were analysed by two-dimensional electrophoresis (the first run: isoelectric focusing, the second run: gradient polyacrylamide-gel-electrophoresis). Haptoglobin (Hp), hemopexin, and one additional protein fluctuated according to their clinical course (e.g. E, P, H type of gestosis). The additional protein was immunologically identified with pregnancy zone protein (PZP). Rabbit monospecific antisera to PZP were produced by using PZP-spots on two-dimensional electrophoresis gels as antigen and succeeding immunoadsorption with healthy non-pregnant women's sera. Quantitation of PZP, Hp and hemopexin was carried out by single radial immunodiffusion (SRID) employing their respective antiserum. Only in severe EPH gestosis, the level of PZP was markedly elevated (approximately 300%), while the level of Hp and hemopexin decrease to 25% and 50% respectively. However, in non-combined merely E, P or H type of gestosis all PZP, Hp nor hemopexin level remained in the normal range.

Furthermore, PZP has been highly purified by a combination of affinity chromatographies of Zn^{++}-column, anti-PZP column and Protein A column, and succeeding FPLC chromatography from pregnant women's sera. Purified PZP induced increased locomotion of polymorphonuclear leukocytes (PMN) but inhibitory locomotion of monocyte (MN) in the phisiological concentration range by using Boyden chambers.

90. Effects of Prostaglandins Inhibitors on Vascular Sensitivity for Angiotensin II in the non-pregnant and the Pregnant Rabbits, in vivo and in vitro (According to the Magnus' Method)

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During pregnancy, the vascular resistance decreases despite the increased circulating blood volume. It is suggested that the changes of Prostaglandins (PGs) system cause this phenomenon to some extent. So we studied the changes of vascular sensitivity especially for Angiotensin II (A-II) under the PGs inhibitors in non-pregnant and pregnant rabbits.

In vivo study: The blood pressure (BP) in the femoral artery and the left renal blood flow (RBF) by the electromagnetic flowmeter were measured in the awaken state about 10 hours after the preparation under fluothane anesthesia. Changes of the estimated renal vascular resistance (RVR=BP/RBF) were evaluated under A-II drip infusion (10^{-6} g/kg·min.) before and after PGs inhibitors (Aspirin as the cyclooxygenase inhibitor: 1, 30, 100 mg/kg, Indomethacin as the same inhibitor: 1 mg/kg, OKY-046 as the specific Thromboxane A_2 synthetase inhibitor: 10, 100 mg/kg).

In vitro study according to the Magnus' method: The isolated spirally cut iliac artery in the non-pregnant or the pregnant rabbits was vertically fixed in Krebs-Henseleit solution and with a force-displacement transducer. A-II was cumulatively dosed (10^{-10}~10^{-6}M). And PGs inhibitors (Aspirin, OKY-046: 10^{-5}~10^{-3}M) were pretreated 7 min. and 3 min. respectively before A-II doses.

The vascular sensitivity for A-II in the pregnant rabbits decreased significantly compared with the non-pregnant as shown by pD_2 values of 8.256 ± 0.037, 8.445 ± 0.044 (m ± SE,-log (M), $p<0.001$) respectively. The effect of Aspirin or Indomethacin did not show the apparent difference from the untreated both in vivo and in vitro, except for low dose of Aspirin in vitro which decreased the vascular sensitivity. However, OKY-046 made the vascular sensitivity decreased both in vivo and in vitro (pA_2 value of >0.2 at $>10^{-4}$M of OKY-046), and this decrease was more extent in the non-pregnant status than in the pregnant.

The Thromboxane A_2 systems are shown to be much corresponded to the vascular sensitivity for A-II, and it is proposed that the favorable effects of OKY-046 could be clinically used as in the PIH cases.

91. Inhibitory Effect of Calcium Channel Blocker on the Contractive Response to Adrenergic Agent in Isolated Arteries from Pregnant SHR

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