



P81 Antibody to Cardiotoxic Steroid Reduces Blood Pressure and Vascular Fibrosis in Preeclampsia

NI Agalakova³, VA Reznik¹, OV Nadei³, IA Ershov¹, OS Rassokha¹, ML Vasyutina², MM Galagudza², AY Bagrov^{1,3,*}

¹Department of Obstetrics and Gynecology, School of Pediatric Medicine

²Institute of Experimental Medicine, Almazov National Medical Research Centre

³Sechenov Institute of Evolutionary Physiology and Biochemistry, St. Petersburg, Russia

ABSTRACT

Background: Previous studies implicated cardiotoxic steroids, including Na/K-ATPase inhibitor marinobufagenin (MBG), in the pathogenesis of preeclampsia (PE). We demonstrated that MBG induces fibrosis via mechanism involving inhibition of Fli1, a nuclear transcription factor and a negative regulator of collagen-1 synthesis.

Objectives and Methods: We hypothesized that PE blockade of increased MBG with antibody would lessen the fibrosis of umbilical arteries and lower the blood pressure in rats with PE. We tested 36 pregnant Sprague-Dawley rats in which 12 were made hypertensive by 1.8% Na supplementation (days 6–19 of gestation), 12 pregnant rats served controls. At day 19, PE rats received one intraperitoneal injection of polyclonal anti-MBG-4 antibody (0.5 ug/mL) for 4 hours.

Results: PE was associated with higher blood pressure (117 ± 2 vs 107 ± 2 mmHg; $p < 0.01$), plasma MBG levels (1.54 ± 0.34 vs 0.49 ± 0.11 nmol/L; $p < 0.01$), protein excretion (26 vs 12 mg/24 hours), sFlt-1 (4-fold), decrease in Fli1 (7-fold) and increase in collagen-1 in aorta (4-fold) vs. control rats (all $p < 0.01$). In 12 rats was treated with polyclonal anti-MBG-4 antibody blood pressure dropped (93 ± 3 mmHg) and Fli1 was decreased much less (2-fold; $p < 0.01$ vs nontreated rats).

Conclusion: These results demonstrate that in experimental PE elevated MBG level is implicated in umbilical fibrosis via suppression of Fli1. Supported by Russian Scientific Foundation grant № 18-15-00222.

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