ENDOTHELIAL DYSFUNCTION IN GESTOSIS/PREECLAMPSIA.

Murashko L and Murashko M.

Research Center of Obstetrics, Gynecology and Perinatology of the Russian Academy of Medical Sciences (Director - Academician of the RAMS, Professor V.I. Kulakov), Moscow, Russia

Dysfunction of the endothelium could have a profound effect on gestosis which is considered by some authors to be a generalized endotheliosis.

MATERIALS AND METHODS: In an attempt to assess the endothelial dysfunction role in the pathogenesis of gestosis 192 pregnant women were enrolled in a study (74 women were evaluated retrospectively and 118 patients - prospectively). In the prospective or main group, gestosis was diagnosed in 75 patients and primary or essential hypertension in 23 women. A comparison group consisted of 20 healthy pregnant women. Special diagnostic methods included daily blood pressure (BP) monitoring and ultrasonic testing of endothelium-dependent vasodilation. NO-metabolites were also evaluated.

Endothelium-dependent vasodilation (EDV) was tested with brachial artery occlusion using ultrasonic control. It was performed for evaluation of endothelial functional activity before and after a 10-14 day-period of antihypertensive therapy.

RESULTS: There was no dependence of the initial brachial artery diameter on gestational age or on gestational pathology. The mean diameter of the brachial artery measured at rest was comparable in healthy women (3.9 mm; 2.9-4.6 mm), in gestosis patients (3.8 mm; 3.0-4.9 mm) and in women with essential hypertension (3.7 mm; 3.0-5.2 mm) ($t<2$; $p>0.005$).

In healthy normotensive pregnant women the mean increase of brachial artery diameter was 19.4% (17.2-25.1%) in the first and second trimesters and 16.4% (14.6-22.3%) in the third trimester. In patients with gestosis, as well as patients with essential hypertension, the EDV data differed reliably from the comparative group. The mean increase of brachial artery diameter in patients with hypertensive disorders due to gestosis and essential hypertension was significantly lower (8.7% and 8.4%, respectively) compared with 11.8% in non-pregnant women and 16.4-19.4% in healthy pregnant women.

Dietary modification in combination with magnesium sulfate and myotropic spasmodic drugs did not influence the endothelium-dependent vasodilation substantially (EDV = 9.0±1.4% compared with 8.9±1.5%). The same tendency was demonstrated using central-acting a-agonists -clonidine and methyldopa (EDV = 8.6±1.3% and 8.5±1.9% compared with 8.4±1.1% and 8.3±1.2% for clonidine and methyldopa, respectively).

We defined dissimilar effects of B-blockers on EDV. Atenolol use was accompanied by the depression of EDV (8.4+1.4% compared with the primary data 8.7±1.1%). In contrast, nebivolol

therapy resulted in a considerable increase of EDV (14.3+1.2% in comparison with 8.6±1.4%). A positive influence on EDV was also noted for the Calcium channel blockers, amlodipine and nifedipine. The increase of EDV after a two-week period of amlodipine and nifedipine use was significantly higher than the initial measurement (12.4+2.1 %; $p<0.005$) and close to the physiological reaction of healthy pregnant women on post-occlusional reperfusion.

We revealed that the level of NO metabolites was significantly higher ($p<0.01$) in patients treated with nebivolol. We also defined that the NO-binding capacity of plasma was reduced significantly in gestosis patients in comparison with healthy pregnant women (19.60±0.92 and 33.86±1.53, respectively). Analyzing daily BP monitoring records in gestosis patients we observed daily circadian oscillations which coincided with analogous dynamics of BP in mice with. modulated gestosis. Our hypothesis that NO concentration is inversely related to BP increase was confirmed in our experiment.

Thus, gestosis is characterized by generalized endothelial dysfunction that is confirmed by a significant decrease of the EDV increment. The lack of NO production as well as decreased NO-binding capacity of plasma can be among the causes of widespread endothelial dysfunction. In gestosis daily circadian BP oscillations are related to NO production. Pharmacological agents with NO-donation can positively influence endothelial dysfunction.

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