EXPERIMENTAL METHODS FOR CLINICAL PRACTICE

Prooxidant-Antioxidant Factors in the Blood of Pregnant Women with Late Gestosis of Different Severity

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Prooxidant-antioxidant factors were studied in the blood of pregnant women with gestosis of different severity. Comparative study showed that activation of peroxidation and decrease in the antioxidant potential depend on the severity of gestosis.

Key Words: *lipid peroxidation; fat-soluble antioxidants; gestosis; severity*

The development of new prognostic and diagnostic criteria for functional activity of metabolic systems in pregnancy complications (*e.g.*, gestosis) is an urgent problem of modern medicine [6,9].

Gestosis is a clinical sign of inadequate adaptive reserves of the maternal organism to meet the fetal demands. Generalized vasospasm, disseminated intravascular coagulation, endothelial dysfunction, inflammation, hypoperfusion, and ischemic dysfunction of organs and tissues are the major pathogenetic stages of gestosis [4,5,8,11].

Oxidative stress is a general nonspecific mechanism for clinical and pathogenetic manifestations of gestosis. The development of oxidative stress is associated with an imbalance between the prooxidant and antioxidant defense components [3]. Gestosis is accompanied by cell membrane destruction. The severity of gestosis is related to the degree of pathological changes [2].

The prooxidant/antioxidant balance at the molecular, cellular, tissue, and organ levels of regulation is important for maintance of homeostatic systems of the female organism during physiological gestation and pathological complications [1,9,13].

Here we studied the prooxidant/antioxidant status of pregnant women as a possible pathogenetic factor of late gestosis and laboratory and diagnostic marker of its severity.

MATERIALS AND METHODS

Eighty-eight pregnant women (20-38 years old) with gestosis of different severity were examined at 30-39 weeks gestation. The severity of gestosis was estimated using a modified scale [6]. Mild, moderate, and severe gestosis was diagnosed in 49 (55.6%), 24 (27.3%), and 15 pregnant patients (17.1%), respectively.

The control group consisted of 22 women with physiological pregnancy. These women were of similar age and gestational period.

Informed consent for the use of these results for scientific purposes was obtained from all pregnant women.

The intensity of lipid peroxidation (LPO) was estimated from malonic dialdehyde (MDA) concentration in blood plasma [12]. MDA level was measured spectrophotometrically in the reaction with thiobarbituric acid. The measurements were performed on a SF-46 spectrophotometer at 532 nm.

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The content of fat-soluble antioxidants (AO), including β-carotene, retinol, and α-tocopherol, in blood plasma was estimated by high-performance liquid chromatography on a Milikhrom chromatograph with UV detection at 260-292 nm [7].

The results were analyzed by Student's *t* test with Bonferroni correction for a confidence level of 95%.

RESULTS

MDA level in blood plasma from pregnant women tended to increase with increasing the severity of late gestosis (from mild to moderate and severe disorder, Table 1).

MDA level in blood plasma from pregnant patients with mild late gestosis was 22.4% higher than in controls. The content of LPO products in the blood from patients with moderate and severe gestosis increased by 25.1 and 35.2%, respectively, compared to the control. Plasma MDA level in severe gestosis was 1.5-fold higher than in mild gestosis ($p<0.05$).

The amount of fat-soluble AO in the peripheral blood from pregnant patients with late gestosis was lower than in pregnant women of the control group (Table 1).

Retinol concentration in pregnant patients with mild and severe gestosis was lower than in control women (by 1.26 and 1.35 times, respectively). Similar results were obtained for plasma β-carotene concentration in patients with moderate and severe gestosis (below the control by 1.45 and 2.05 times, respectively). The concentrations of β-carotene and retinol in pregnant patients decreased with increasing the severity of gestosis.

It should be emphasized that plasma α-tocopherol concentration increased in mild gestosis (by 1.21 times), but decreased in severe gestosis (by 1.33 times, $p<0.05$).

Variations in α-tocopherol concentration depend on the severity of late gestosis in pregnant patients, which probably serves as an adaptive response to activation of LPO in the blood. These features are probably associated with redistribution of α-tocopherol from the liver and adipose tissue into the blood. It is induced by an increase in oxidative reactions in the circulatory system, which results from activation of enzymes for generation of reactive oxygen and nitrogen metabolites (NADPH oxidases, xanthine oxidases, and NO synthases) and elevation of lipoprotein concentration [3]. These changes probably accompany the development of late gestosis in pregnancy.

The regulation of peroxidation by AO (primarily by α-tocopherol) is mediated by a feedback mechanism [2,7]. The AO/LPO product ratio should be maintained at a constant level to provide the physiological balance. This level is associated not only with activity of the LPO-regulating system, but also with metabolic processes in the organism.

We calculated the AO/LPO ratio (α-tocopherol/MDA ratio). Pregnant patients with mild gestosis were characterized by increased blood α-tocopherol concentration, but had normal α-tocopherol/MDA ratio. However, further increase in the severity of disease was accompanied by a prooxidant/antioxidant imbalance.

The α-tocopherol/MDA ratio in pregnant patients with moderate and severe gestosis was lower than in control women (by 1.53 and 2.08 times, respectively). These data suggest that the progression of gestosis is accompanied by LPO activation. Excessive formation of LPO products impairs the barrier and matrix function of cell membranes. Impaired barrier function in membrane lipid bilayer is associated with changes in activity of ion channels (primarily of Ca^{2+} channels). Massive influx of calcium ions into the cell is followed by irreversible changes, including energy deficiency and apoptosis [2]. This mechanism probably mediates the involve-

TABLE 1. Content of LPO Products and Fat-Soluble AO in Blood Plasma from Pregnant Patients with Late Gestosis of Different Severity (*M*±*m*)

Parameter, μmol/liter	Control (*n*=22)	Severity of gestosis		
		mild (*n*=49)	moderate (*n*=24)	severe (*n*=15)
MDA	3.16±0.09	3.87±0.20*	4.52±0.26*	4.93±0.19*
β-Carotene	0.42±0.02	0.37±0.04	0.31±0.05*	0.22±0.05*
Retinol	0.87±0.03	0.69±0.04*	0.72±0.08	0.64±0.07*
α-Tocopherol	22.8±0.11	27.5±0.09*	21.30±0.07	17.10±0.08*
α-Tocopherol/MDA	7.21±0.19	7.11±0.17	4.71±0.20*	3.47±0.18*

Note. *$p<0.05$ compared to the control.

ment of peroxidation in damage to the central nervous system, kidneys, uterus, and liver during gestoses [6].

We conclude that prooxidant/antioxidant imbalance in the organism due to activation of LPO and AO deficiency is a general nonspecific pathogenetic factor of late gestosis. Blood components (MDA, β-carotene, retinol, and α-tocopherol) can be used as additional laboratory and diagnostic markers of the severity of late gestosis in pregnant patients.

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