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ROLE OF THE ENDOTHELIAL SYSTEM IN THE DEVELOPMENT OF HYPERTENSION IN PREGNANT WOMEN

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Abstract
In recent years, the role of the vascular endothelium in the pathogenesis of the development of critical conditions, including the development of gestational complications, has received increasing attention. This review presents current literature data on the role of endothelial dysfunction in the development of hypertensive conditions during pregnancy.

Keywords: Pregnancy, hypertension, preeclampsia.

Introduction

In recent years, increasing attention has been paid to the role of vascular endothelium in the pathogenesis of critical conditions, including the development of systemic inflammatory response syndrome and multiple organ failure [3,12].
Insufficient understanding of the pathogenesis of preeclampsia significantly limits the development of reliable prognostic diagnostic methods and effective preventive measures. Due to its close relationship with the pathophysiology of preeclampsia, vascular endothelial dysfunction has attracted considerable research interest. One of the most extensively studied approaches to assessing endothelial function is the measurement of specific biochemical markers in the blood, whose concentrations increase in pathological pregnancy.
Endothelial cells of blood vessels perform a wide range of functions. They ensure blood fluidity and prevent contact between blood components and subendothelial procoagulants through the expression of various membrane-bound heparin-like molecules, tissue factor inhibitors, and thrombomodulin. Endothelial cells synthesize mediators that regulate vascular tone and produce anticoagulant and anti-adhesive substances [8]. Being in close contact with circulating blood,

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endothelial cells participate in the activation of the coagulation system, and their damage is directly associated with organ dysfunction [1,3,6].

It has been established that the endothelium is a site of synthesis of biologically active substances exerting both vasodilatory and vasoconstrictive effects. Vascular endothelium also possesses anticoagulant, antiplatelet, and fibrinolytic activity through the synthesis of prostacyclin, nitric oxide, tissue plasminogen activator, urokinase, thrombomodulin, and proteins C and S [10–13].

As is well known, the dominant clinical syndromes of preeclampsia include arterial hypertension and disturbances of water–electrolyte balance, which are accompanied by multiple organ failure as the severity of the condition increases [6,7]. An important role in the mechanisms of microcirculatory disorders in preeclampsia is attributed to changes in the coagulation potential and rheological properties of blood [8,9], the pathogenetic mechanisms of which require further clarification. In particular, the role of endothelial dysfunction in the impairment of regional blood flow and microcirculation in various organs and tissues in preeclampsia remains insufficiently studied.

The results of our study indicate that disturbances in the coagulation potential of blood in patients with moderate and severe preeclampsia are associated with the development of endothelial dysfunction.

Establishing a pathogenetic relationship between the severity of clinical manifestations of preeclampsia, endothelial dysfunction, and disorders of blood coagulation potential allows the recommendation of new criteria for diagnosis and prognosis of the course of this gestational pathology. For this purpose, monitoring of hemostasis parameters, as well as plasma levels of endothelin-1, thrombomodulin, thrombospondin, intercellular adhesion molecules, and nitric oxide metabolites is required.

In preeclampsia, damage to endothelial cells leads to the release of endothelin-1 [23]. Accordingly, increased concentrations of endothelin-1 in peripheral blood, combined with activation of intravascular coagulation, result in impaired circulation in the brain, liver, heart, kidneys, and other organs, leading to the development of local tissue hypoxia [19].

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In preeclampsia, almost all endothelial functions are impaired, including regulation of vascular tone, immune processes, and vascular permeability.

Methods for assessing endothelial function using biochemical markers have not been widely implemented in clinical practice due to their nonspecificity and significant variability depending on external conditions (time of testing, patient condition, presence of concomitant inflammatory diseases, etc.). At the same time, functional tests for assessing endothelium-dependent vasodilation are considered promising for predicting preeclampsia, especially when combined with other specific markers of pregnancy pathology.

The results of studies evaluating endothelium-dependent vasodilation in preeclampsia are inconsistent and often contradictory. Several studies have demonstrated that endothelial function in gestational hypertension (without proteinuria) may be accompanied by an increased vasodilatory response compared with normal pregnancy [20,21], which is traditionally associated with increased cardiac output in the setting of hypertension [22]. Many authors have reported a marked impairment of endothelium-dependent vasodilation in patients with preeclampsia compared both with healthy pregnant women and non-pregnant women. Moreover, recent studies suggest that the presence of endothelial dysfunction diagnosed by reactive hyperemia testing in healthy pregnant women may serve as a predictor of future development of preeclampsia. In the study by B. Takase et al. [23], 43 women (mean age 32 ± 5 years) in the second half of pregnancy were included. All participants had a relatively high risk of developing preeclampsia: 12 had a history of preeclampsia, 3 had first-degree relatives with preeclampsia, and 2 had preexisting kidney disease. Subsequently, preeclampsia developed in 9 women, while 34 remained normotensive. Endothelial function was assessed using a reactive hyperemia (occlusion) test. The increase in brachial artery diameter after occlusion was measured by ultrasound. Regardless of subsequent development of preeclampsia, the groups were comparable in terms of traditional risk factors. Baseline plasma levels of endothelin-1 and asymmetric dimethylarginine were similar in both groups. Only endothelium-dependent vasodilation was significantly reduced in women who developed preeclampsia compared with healthy pregnant women (1.6 ± 1.0% vs.

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11.0 ± 4.5%; $p < 0.05$). An increase in brachial artery diameter of less than 3.0% in the second half of pregnancy demonstrated a positive predictive value of 90% and a negative predictive value of 100% for subsequent development of preeclampsia [23].

Similar results were obtained by R. Kamat et al. [24]. Women with lower increases in brachial artery diameter after occlusion had a significantly higher risk of developing gestational hypertension. The test demonstrated high sensitivity (88%) and specificity (93%).

The largest study was conducted by R. Garcia et al. [25], involving 506 normotensive pregnant women. Those who later developed gestational hypertension showed significantly lower endothelium-dependent vasodilation compared with women who remained normotensive throughout pregnancy (13.4 ± 4.3% vs. 18.2 ± 7.12%; $p < 0.05$).

Further studies confirmed the prognostic significance of impaired endothelium-dependent vasodilation and its dynamic changes during pregnancy in predicting preeclampsia [26–28].

Conclusions

According to current literature, endothelial dysfunction plays a key role in the pathogenesis of hypertensive disorders during pregnancy and may have significant diagnostic and prognostic value in the prevention of pregnancy-related complications.

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