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ETIOPATHOGENETIC MECHANISMS IN PRE-ECLAMPSIA

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Abstract:

The article under discussion reveals the etiopathogenetic mechanisms in pre-eclampsia. The author believes that placenta-associated complications of pregnancy (pre-eclampsia and eclampsia) and concomitant placental insufficiency are among the main causes of maternal and perinatal morbidity and mortality. Identification of a high-risk group of placenta-associated complications, selection of adequate management tactics for pregnant women with placenta-associated complications, taking into account the pathogenetic mechanisms of pre-eclampsia is the basis for effective prevention of adverse perinatal outcomes in placenta-associated complications.

Keywords: Pre-eclampsia, eclampsia, placenta-associated complications, generalised vasospasm, placental perfusion, hypertension.

INTRODUCTION

Preeclampsia a complication of pregnancy due to the mismatch between the ability of the adaptation systems of the mother's body to adequately meet the needs of the developing foetus. It is a complex neurohumoral process manifested by various disorders of the central and autonomic nervous, cardiovascular and endocrine systems, as well as disorders of a number of metabolic processes, immune response and other functions of the pregnant woman's body [8].

THE MAIN PART

Pathogenetic mechanisms of pre-eclampsia

The primary element is abnormal trophoblast invasion in early pregnancy. This in turn provokes the release of substances into the mother's bloodstream, leading to the development of endothelial dysfunction and activation of growth factors: proteases, interleukins (IL-1, IL-6, TNF-a, imbalance between vasoconstrictors and endothelial vasadilators), disorders of lipid and fatty acid oxidation processes [1].

The genesis of pre-eclampsia is based on generalised vasospasm, leading to increased peripheral vascular resistance and subsequent reduction in perfusion of vital organs (brain, liver, kidneys, placenta).

Reduced placental perfusion can lead to delayed growth and development of the foetus and is the main cause of perinatal morbidity and mortality. Reduction of uteroplacental blood flow by 50-60% occurs 3-4 weeks before the moment when hypertension becomes obvious [4].

Reduced renal blood flow and glomerular filtration is the cause:

- hypoxia of the tubules and consequent proteinuria, water retention and oedema;
- increase in plasma concentration of uric acid, creatinine, urea (in severe cases).

Haemoconcentration as a result of increased vascular permeability with a decrease in intravascular fluid (hypovolemia) and signs of growth of extravascular (interstitial oedema).

Pathological hypercoagulability, expressed primarily in the increase in platelet aggregation.

Disturbance of production and decay of prostacyclin/thromboxane - prostaglandins, which have an opposite effect on vascular tone and platelet aggregation.

Vascular endothelial damage is caused by:

- increased activity of the cellular and humoral links of immunity in response to particularly active antigens of the foetus, necessary for the formation of the cerebral cortex from 20-22 weeks of pregnancy. Formed immune complexes "settle" on the walls of blood vessels, damaging the endothelium. Anti-phospholipid antibodies also cause damage to the endothelium, which leads to a decrease in the synthesis of nitric oxide, relaxing the vascular wall, increased production of cytokines and eicosanoids, increased vascular permeability, increased sensitivity to endogenous vasopressors;
- mediators of systemic inflammatory response syndrome, which always develops in the body of pregnant women with gestosis.

Extremely important for practitioners are the concepts of "pregnancy norm" and "norm of compensated pathology" in gestosis. The norm of pregnancy is a complex of physiological restructuring in all organs and systems in the body of a pregnant woman, aimed at prolongation and successful completion of the gestational process. In normal pregnancy is observed hypervolemic autohemodilution

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due to an increase in CCA by 30%, mainly due to the plasma component. As a consequence, the rheological properties of blood are improved: viscosity decreases, fluidity increases. Hemoglobin and haematocrit decrease to the lower limit of the normal zone. There is the so-called relative anaemia of pregnant women [6].

Under the influence of hormones of the feto-placental complex, including progesterone, in physiological pregnancy are vascular hypotension, physiological hypercoagulability and immunosuppression. There is a relaxation of smooth muscle bronchioles, GI tract and urinary tract. Increasing in size uterus contributes to changes in the topographic-anatomical relationships of the abdominal and thoracic cavity organs, compresses the pelvic sections of the ureters and the inferior vena cava. Cholestasis, constipation, dynamic and mechanical ureteral obstruction are often noted in pregnancy. Inferior vena cava compression syndrome contributes to a significant decrease in venous return to the left ventricle, which leads to a sharp decrease in stroke and minute volumes of the heart. Clinically, it is manifested by a decrease in BP and tachycardia. In severe cases, the blood circulation in the system mother - placenta - foetus is disturbed, there may be premature detachment of the placenta. Therefore, during pregnancy it is very important to limit the position during rest on the back, as well as travelling in transport on seats with vertically raised backrest [7].

Under the concept of "compensated pathology norm" means changed towards pathology clinical and laboratory indicators of homeostasis of the pregnant woman without the presence of decompensation. Gestosis occurs within the clinical form of mild preeclampsia. In this case, no drug correction is required. If the doctor tries to carry out correction, i.e. prescribe symptomatic treatment, he will get the worst result for both mother and foetus.

Table 1 shows clinical and laboratory indicators of homeostasis in physiological and complicated gestosis pregnancy, which do not require drug therapy.

Table 1. Some indicators of homeostasis in normal and complicated gestosis pregnancy.

Indicator	**Pregnancy norm**	**The norm of compensated pathology in gestosis**
HR	80-85 per 1 min.	90-100 per 1 min.
CAD	95 mm Hg	100-120 mm Hg
CVD	50-120 mmHg	35-50 mm Hg
ODC Haematocrit	82.2 ml/kg 34-36 l/l	75 ml/kg (not lower) 36-38 l/l
Haemoglobin	112-120 g/l	120-125 g/l
Lymphocytes	20-28 %	19% at least
Total protein	62-64 g/l	60-62 g/l
Prothrombin	100-110 %	90-100 %
Fibrinogen	2-4 g/l	1.5-2 g/l
Platelets	200-400 ths	140-200 ths.
Creatinine	47-51 μmol/l	56-90 μmol/l
Plasma urea	2-5 mmol/l	5-7 mmol/l
Plasma sodium	134-137 mmol/l	140-145 mmol/l
Plasma osmolarity	279-283 mosmol/kg	290-310 mosmol/kg

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Plasma cortisol	160-840 mmol/l	840-1000 mmol/l
Urine protein	0	less than 0.3 g/day
Daily urine volume	1050-1800 ml/d	800 - 1000 ml/day

Compensation factors in gestosis:

- K1 = CAD / HR = 1-1.5 normal
- K2 = HR / HR = 4.5 normal
- an increase in K1 over 1.5 and K2 over 4.5 indicates a decompensated course of gestosis.

The use of these simple coefficients, allows in any conditions to identify decompensation and timely decide on the active tactics of management of the pregnant woman. Always remember that the only pathogenetically justified method of treatment of pregnant women with severe gestosis is delivery.

The earliest symptom of gestosis - oedema. It is known that swelling of the lower extremities is considered as a physiological phenomenon. Edema is considered a symptom of gestosis when it is generalised after 12 hours of bed rest or due to weight gain.
or due to weight gain of more than 350g per week, especially in combination with nicturia and decreased diuresis. According to the prevalence of oedema distinguish 4 degrees:

degree I - oedema of the lower extremities only;

degree II - oedema of the lower extremities and abdomen;

degree III - oedema of the lower extremities, abdomen and face;

degree IV – anasarca.

Severe pre-eclampsia usually precedes eclampsia. It is characterised by impaired function of vital organs with predominant CNS damage. Pregnant women usually complain of headache, a feeling of heaviness in the occipital region, visual disturbance (appearance of flies or fog before the eyes), nausea vomiting, pain in the epigastric and lumbar region (Zangemeister's symptom), or in the right subcostal region.

Eclampsia is a severe form of gestosis, which is characterised by a complex symptom complex in which there is a generalised spasm of cerebral vessels, as well as cerebral edema, which leads to increased intracranial pressure and impaired cerebral blood circulation and, ultimately, to ischaemic and haemorrhagic damage to brain structures.

The most typical symptom of eclampsia is the presence of convulsions of the transverse striated muscles of the whole body. However, there is also a convulsion-free form of eclampsia - eclamptic coma, the prognosis for which is particularly unfavourable. The seizure attack lasts on average 1-2 minutes and consists of the following stages. At first, there are small fibrillary twitches of the facial muscles, which later spread to the upper extremities. Then comes a period of tonic convulsions, which lasts 15-25 seconds. The patient does not breathe during the seizure, cyanosis increases. This is the most dangerous period as death from cerebral haemorrhage may occur. Following the period of tonic convulsions, there comes a period of clonic convulsions spreading all over the body from top to bottom. The patient is not breathing. Gradually the convulsions become more infrequent and weak and stop. The patient takes deep noisy breaths accompanied by snoring. Breathing becomes deep but infrequent. Clonic convulsions last from 30 seconds to 1.5 minutes. The resolution period is characterised by the fact that the patient regains consciousness. She does not remember anything about what happened. Blood-coloured foam is emitted from the mouth. Usually she complains of headache and a feeling of brokenness. Sometimes the seizures alternate one after the other without a period of resolution (eclampsic status). Coma may also develop due to cerebral oedema [3].

Differential diagnosis of gestosis should be carried out with glomerulonephritis, chronic arterial hypertension, epilepsy and other diseases leading to acute disruption of cerebral circulation (thrombosis or rupture of cerebral vessels in aneurysms, brain neoplasms).

Complications of the disease

Complications of severe forms of gestosis should include the development of multi-organ failure, oedema and/or brain haemorrhage. In severe, especially combined, gestosis is marked by the development of secondary feto-placental insufficiency, which contribute to delayed growth and development of the foetus, chronic intrauterine hypoxia, high rates of perinatal morbidity and mortality. Severe forms of gestosis pose a real threat to the life of the mother.

General principles of management of pregnant women with gestosis

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The goals of treatment are prevention of pre-eclampsia and eclampsia, restoration of functions of vital organs, timely delivery. Treatment of pregnant women on an outpatient basis is allowed in the case of oedema of the degree I. With oedema degree II-IV, gestosis treatment is carried out in hospital. And severe forms - in the conditions of perinatal centres and obstetric hospitals at multidisciplinary hospitals. Abroad (USA), pregnant women with mild pre-eclampsia are observed and treated on an outpatient basis, which has a significant economic effect. It seems to us that with the introduction of the position of a general practitioner who can carry out daily monitoring of the pregnant woman, such an opportunity will appear. But the following conditions must be fulfilled. The family doctor must make sure that a pregnant woman with mild pre-eclampsia gives an adequate assessment of her condition, is well informed about possible complications, lives in a full-fledged family with good material and living conditions, has the ability to independently monitor BP, urine protein, daily diuresis, oedema, weight gain, fetal motor activity. The GP should draw the patient's attention to the need for hospitalisation in case of increasing symptoms of gestosis by ambulance or private transport, but with the compulsory accompaniment of the GP. The decision on the possibility of outpatient management of a pregnant woman with mild pre-eclampsia is jointly made by the obstetrician-gynaecologist of the antenatal clinic and the general practitioner. If the above conditions cannot be met, the pregnant woman must be hospitalised.

CONCLUSION

The provision of medical care is presented as a sequence of the following stages:

1. Women's clinic. Family doctor's office:
   - assessment of the pregnant woman's condition, diagnosis;
   - creation of an examination plan and management plan for pregnant women at risk, observation and assessment of the pregnant woman's condition, decision on the choice of a hospital for delivery;
   - if there are good conditions joint management of patients with a mild form of GWB (in the absence of conditions-hospitalisation) is allowed.
2. Maternity ward (maternity hospital):
   - pregnancy pathology department or ward - treatment of mild to moderate forms of GWB;
   - the intensive care unit or PIT - treatment of severe forms of GVB and eclampsia.
3. Rehabilitation of maternity women who have undergone gestosis in the therapeutic department, clinic, antenatal clinic, training for planning the next pregnancy.

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