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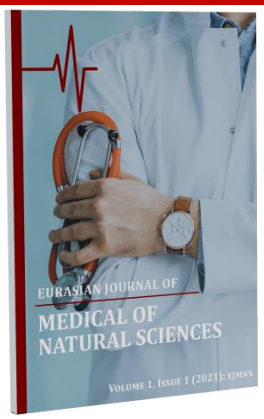

CLINICAL PHARMACOLOGICAL APPROACH TO RATIONAL TREATMENT OF PREGNANT WOMEN WITH PREECLAMPSIA

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ABSTRACT

A total of 105 pregnant women with gestosis of varying severity and 35 women with uncomplicated pregnancy were examined. The study method was the study of the state of central and peripheral hemodynamics. Multidirectional changes in PWV, Part after the pharmacological test by 19% or more indicate the absence of ED, by 12-19% - insignificant ED and mild gestosis, by 6-12% - moderate ED and moderate gestosis; the absence of changes in vascular parameters is characteristic of severe gestosis and generalized endotheliosis.

INTRODUCTION

In modern obstetrics, gestosis remains one of the most formidable complications of pregnancy. Despite the developed and adopted preventive measures, its frequency does not decrease and, according to various authors, ranges from 7 to 27% [1]. In the structure of maternal mortality, gestosis ranks 3rd, being the direct cause of death in 11.8-14.8% of cases. Perinatal morbidity in gestosis is 640-780‰, mortality is 18-30‰ [1, 3, 4]. Reducing the level of maternal and perinatal morbidity is a priority task at all stages of obstetric care [1, 2, 3, 5].

Currently, the leading role in the pathogenesis of gestosis is given to vascular disorders and microcirculation disorders, leading to systemic hemodynamic shifts in the body of a pregnant woman [1, 3]. The main pathogenetic aspect in gestosis is endothelial dysfunction. Therefore, in modern conditions, to prevent severe forms of gestosis, the patient's condition should be assessed taking into account not only clinical manifestations, but also laboratory and instrumental indicators. Registration of changes occurring in the vascular system during gestosis is now possible with the help of a new diagnostic method based on volumetric compression oscillometry, implemented in the KAP-CG-osm "Globus" device. This device makes it possible to determine the indicators of peripheral hemodynamics, which characterize changes in the vascular system and help to identify gestosis at the subclinical stage. These indicators include pulse wave velocity and brachial artery compliance, which allow us to determine the rigidity and elastic-viscous properties of individual vessels and the vascular system as a whole.

MATERIALS AND METHODS

A comprehensive examination of 105 patients with gestosis was conducted. The comparison group consisted of 35 women with a physiological pregnancy, examined at periods from 20 to 41 weeks of pregnancy. According to the Goecke assessment scale modified by G. M. Savelyeva (2000), mild gestosis (subgroup I) was present in 30 pregnant women, moderate gestosis (subgroup II) occurred in 30 pregnant women, severe gestosis and preeclampsia (subgroup III) - in 30, eclampsia (subgroup IV) - in 15 patients. The average age of women with uncomplicated pregnancy was 24.7 ± 0.6 years (hereinafter, all average numerical values are given as M ± SD). The average gestational age at the time of delivery was 39.6 ± 0.4 weeks. All births were uncomplicated and resulted in the birth of live, full-term infants with an Apgar score of 8–10. The average birth weight of the infants was 3498±288 g.

RESULTS AND DISCUSSION

The average age of the subjects in the main group was 25.9±6.6 years and did not differ significantly from the same indicator in the comparison group. However, severe gestosis developed significantly more often in the group of young primiparous women (under 18 years) and older pregnant women (over 35 years). It should also be noted that in the subgroup of patients with severe gestosis and preeclampsia, primiparous women (68.3±4.3%), women with a history of habitual miscarriage (26.6±3.8%), and a long interval between births (9.5±2.4%) predominated. In the structure of extragenital pathology, somatic diseases predominated in the main group (56.2%) compared to the control group (8.6%). In the group with gestosis of varying severity, a high frequency of anemia (30.1%), kidney pathology (37.5%), gastrointestinal diseases (21.6%), and obesity (24.1%) were established. Pregnant women with hypertension were not included in the study.

In the main group, the course of the current pregnancy was complicated by gestosis in the first half of pregnancy in 35 (33.3%) women, the threat of termination of pregnancy in the first trimester - in 43 (41%), placental insufficiency - in 90 (85.7%), polyhydramnios - in 24 (22.9%), oligohydramnios - in 25 (23.8%), fetal growth retardation syndrome - in 67 (63.8%). Monosymptomatic gestosis in the form of arterial hypertension was detected in 31.7% of those examined in the main group, and only 24.7% of patients with gestosis had the classic Zangemeister triad. In the subgroup with mild gestosis, 86.6% of patients delivered on time, 6.7% of pregnancies ended in premature birth, and 6.7% in late birth. In the subgroup with moderate gestosis, 80% delivered on time and 20% delivered prematurely. In the subgroup with severe gestosis, 60% delivered on time and 40% delivered prematurely. In the subgroup with eclampsia, the ratio of timely and premature births was almost the same — 53.3% and 46.7%, respectively. In the control group, all pregnancies ended in timely birth. The main indications for cesarean section in the main group were: severe gestosis and preeclampsia - in 61.6%, progression of gestosis against the background of adequate therapy - in 32.2%, increasing severity of fetoplacental insufficiency, according to Doppler study data - in 15.4% of patients.

When studying vascular parameters (PWV, Part) in pregnant women with gestosis and during physiological pregnancy, the following patterns were discovered. In the control group, the PWV value was 801.914±51.822 cm/sec, while in the subgroups with mild gestosis - 1028.733±55.422 cm/sec; average - 1074.333±53.899 cm/sec; severe gestosis and

preeclampsia - 1122.000±70.663 cm/sec; eclampsia - 1443.600±116.500 cm/sec. Having studied the values of Part, we obtained the following data: in the control group this indicator was 0.131±0.064 mm/mm Hg, and in the main group - 0.055±0.007 mm/mm Hg, which corresponded to mild gestosis; 0.056±0.009 mm/mm Hg - moderate; 0.055±0.009 mm/mm Hg - severe gestosis and preeclampsia; 0.048±0.005 mm/mm Hg - eclampsia.

Based on the data we have obtained, Part can be considered an indicator of gestosis manifestation. This is confirmed by the fact established by many authors that long before the clinical manifestations of gestosis, a complex pathogenetic mechanism for the formation of endothelial dysfunction is launched in the intima and subendothelial layer of the arteries. Changes in the endothelium during gestosis consist of swelling of the cytoplasm with the deposition of fibrin around the basement membrane, and endotheliosis develops inside the swollen endothelial cytoplasm [3]. Therefore, a more in-depth study of the early mechanisms of endothelial dysfunction formation during gestosis is of great importance.

Considering the importance of endothelial dysfunction in the pathogenesis of gestosis, markers indicating endothelial damage may be of great diagnostic value. Our study showed that vascular parameters (PWV, Part) may be considered as such markers, since pregnant women with gestosis had significantly ($p<0.05$) higher levels of PWV and lower Part compared to healthy pregnant women; their levels moderately correlated with the severity of gestosis (RSPV=0.612, RPart=–0.514), the time of onset and duration of the course (RSPV=0.412, RPart=–0.314), the severity of the main clinical symptoms: edema (RSPV=0.347, RPart=–0.311), proteinuria (RSPV=0.513, RPart=–0.307), hypertension (RSPV=0.701, RPart=–0.351). In case of placental blood flow impairment, higher levels of RSPV and low levels of Part were also determined.

The inaccessibility of structural disorders of the endothelium for direct study dictates the need to search for sensitive methods for determining endothelial dysfunction, given its important role in the genesis of hemovascular disorders in pregnant women. The method for studying the function of the endothelium of peripheral arteries in our study was based on the assessment of changes in vascular parameters in response to a pharmacological test with nitroglycerin. This drug was considered as an exogenous source of nitric oxide. The proposed method using a nitric oxide (NO) donor is designed to monitor the guanylate cyclase mechanism of vasodilation and identify the initial manifestations of endothelial dysfunction. To diagnose NO-guanylate cyclase endothelial dysfunction, hemodynamic parameters were studied, namely:

— monitoring the degree of increase (decrease) in PWV in response to the effect on the body of endothelium-dependent and -independent stimuli;

— monitoring the degree of increase in vascular wall compliance in response to the effect on the body of endothelium-dependent and -independent stimuli.

The PWV values in all subgroups significantly ($p<0.05$) differed from the control group and between themselves. The Part values in all subgroups significantly ($p<0.05$) differed from the control group, and reliable differences were also revealed between the subgroups with mild gestosis and preeclampsia. Thus, a decrease in the pulse wave growth, an improvement in the brachial artery compliance indices by 19% or more from the initial level in response to the action of an endothelium-dependent pharmacological stimulus indicate the preservation

of the NO-guanylate cyclase mechanism of vasodilation and the absence of gestosis. A change of 12-19% corresponds to a mild course of gestosis and minor endothelial dysfunction, a change of 6-12% corresponds to moderate severity of gestosis and moderate endothelial dysfunction. The absence of changes in vascular parameters (brachial artery compliance, pulse wave velocity, vascular wall compliance, the ratio of actual specific peripheral resistance to working resistance) was interpreted as a sign of generalized endotheliosis, and, consequently, severe gestosis. Analysis of the degree of changes in PWV, vascular wall compliance in response to nitroglycerin administration makes it possible to judge the preserved or suppressed guanylate cyclase activity of the muscular layer of blood vessels, and, consequently, the degree of endothelial dysfunction.

CONCLUSION

Our study revealed that with increasing severity of gestosis, the indicators characterizing the state of the vascular wall change: indicators of peripheral vascular resistance (PVR) increase, and indicators characterizing the throughput capacity of the vascular bed (Part) significantly decrease, which proves the occurrence of “hypoperfusion” syndrome against the background of endothelial damage in gestosis.

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