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CONTEMPORARY PERSPECTIVES ON THE PROPHYLAXIS OF HYPERTENSIVE DISORDERS OF PREGNANCY: ASSESSING THE EFFICACY OF COMBINED PREVENTIVE APPROACHES IN HIGH-RISK POPULATIONS

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Hypertensive disorders of pregnancy (HDP) remain one of the leading causes of maternal and perinatal morbidity and mortality worldwide, despite continuous improvements in obstetric care [1-3]. Physiological pregnancy is accompanied by profound cardiovascular, metabolic, and immunological adaptations, the adequacy of which largely depends on the balance between the generation of reactive oxygen and nitrogen species, the effectiveness of antioxidant defenses, and sufficient bioavailability of nitric oxide (NO). Disruption of redox homeostasis results in excessive accumulation of free radicals, damage to cellular structures, and progression of endothelial dysfunction [4-6]. L-arginine, the principal substrate for NO synthesis, is considered a promising agent for improving vasodilation and uteroplacental perfusion [7]. In this context, combining agents that concurrently enhance NO-dependent mechanisms and the organism’s antioxidant capacity appears biologically plausible and may more effectively prevent early disturbances in vascular regulation.

Objective: To evaluate the effectiveness of prophylactic approaches for preventing hypertensive disorders of pregnancy in high-risk women and to assess their impact on delivery outcomes.

Materials and methods

The study was conducted at the clinical site of the Municipal Non-Commercial Enterprise "Regional Perinatal Center" of the Zaporizhzhia Regional Council. A total of 64 pregnant women in their first trimester, who met the criteria for high risk of developing hypertensive disorders of pregnancy according to current clinical guidelines of the Ministry of Health of Ukraine, were enrolled. Following an initial clinical assessment, all participants were randomized by simple random sampling into two equal groups of 32 women each: C1 and C2.

Group C1 received the standard prophylactic regimen, which included acetylsalicylic acid at a dose of 150 mg/day from 12 to 36 weeks of gestation and calcium at a dose of 1–2 g/day starting from 16 weeks, along with an additional combined prophylactic therapy. The combined regimen consisted of L-arginine aspartate (200 mg/mL, 5 mL three times daily for 14 days) and a micronutrient complex with antioxidant and endothelioprotective properties (folic acid 400 μg, cholecalciferol 5 μg, docosahexaenoic acid 200 mg, vitamin E 12 mg, potassium iodide 150 μg once daily). Group C2 received only the standard prophylaxis recommended by the Ministry of Health of Ukraine.

The clinical assessment included evaluation of clinical data, obstetric-gynecological history, and somatic history. All examinations adhered to the requirements of the national regulatory documents of the Ministry of Health of Ukraine, including the current medical care standard "Normal Pregnancy" (Order No. 1437, dated August 9, 2022) and the Unified Clinical Protocol "Hypertensive Disorders of Pregnancy" (Order No. 151, dated January 24, 2022).

Evaluation of the fetoplacental unit was performed using standard ultrasound fetometry and Doppler studies. Doppler indices of vascular resistance were interpreted in accordance with the percentile ranges defined by the Fetal Medicine Foundation.

Results

The comparative sample included 64 pregnant women who were statistically homogeneous across the main clinical parameters ($p>0.05$). The mean age of the participants was 31.09 ± 5.45 years, with a median of 30.5 [27-36] years. The distribution of occupational categories was balanced, with no statistically significant differences between the groups ($p>0.05$).

Parity characteristics were balanced: 39.1% of pregnancies were first pregnancies, while 60.9% were subsequent. First births accounted for 56.2% and repeated births for 43.8%. Previous medical abortions were reported by 18.8% of women, spontaneous miscarriages by 9.4%, and preterm birth in history by 6.3%. Overall, the cumulative frequency of pregnancy losses was low (16 medical and 10 spontaneous abortions).

Extragenital pathology (EGP) was documented in 84.36% of the women. Metabolic disorders were most common, including overweight (76.6%) and obesity (25.0%). Ophthalmologic conditions were represented mainly by myopia (15.6%), with isolated cases of retinal angiodystonia (1.6%) and complex myopic astigmatism (3.1%). Somatoform autonomic dysfunction was frequent (43.8%). Among cardiovascular disorders, mitral valve prolapse (14.1%) and varicose disease of the lower limbs (15.6%) were most prevalent. Other EGP included chronic pyelonephritis (10.9%), nontoxic goiter and hypothyroidism (15.6%), dorsopathies (10.9%), as well as isolated cases of urolithiasis (1.6%), chronic cholecystitis (3.1%), and chronic cytomegalovirus infection (9.4%).

Gynecological disorders were recorded in 39.1% of participants. Cervical erosion/ectopy was most frequent (31.3%), followed by mild cervical dysplasia (10.9%) and ovarian cysts (9.4%). Isolated cases of PCOS, ectopic pregnancy, and uterine scarring were observed. Most women (90.6%) had regular menstrual cycles.

Among high-risk factors, the most common were a history of HDP (35.9%) and an adverse obstetric history in the participant's mother (18.8%). Moderate risk factors included age over 35 years (37.5%), BMI >30 kg/m² (25.0%), primigravidity (32.8%), and a family history of hypertension (28.1%). The prevalence of individual risk factors did not differ between C1 and C2 ($p>0.05$).

The incidence of HDP was substantially lower in the combined prophylaxis group. In C1, HDP developed in 5 of 32 women (15.6%) – 2 cases of moderate preeclampsia and 3 cases of gestational hypertension; no severe preeclampsia was recorded. In C2, HDP occurred in 12 of 32 participants (37.5%), including 5 cases of moderate, 1 case of severe preeclampsia, and 6 cases of gestational hypertension. Accordingly, the proportion of women without HDP was 84.4% in C1 versus 62.5% in C2.

Prepregnancy and third-trimester body weight and BMI were comparable between groups ($p>0.05$). The mean prepregnancy BMI was 22.17 kg/m² in C1 and 22.92 kg/m² in C2; in the third trimester, 27.40 and 27.28 kg/m², respectively.

A wide spectrum of gestational complications, typical for high-risk HDP populations, was observed. The most frequent condition was maternal anemia: 53.1% in C1 and 62.5% in C2. Threatened miscarriage before 22 weeks occurred in 21.9% of C1 and 37.5% of C2; cervical insufficiency in 6.3% and 12.5%, respectively. Threatened preterm labor (false contractions before 37 weeks) was observed in more than two-thirds of the entire cohort. More severe complications – including preterm premature rupture of membranes and placental abruption – were documented only in the standard prophylaxis group. However, the overall frequency of gestational complications did not differ significantly between groups ($p>0.05$).

Third-trimester Doppler findings showed normal blood flow in 68.8% of women in C1 and 59.4% in C2. Terminal hemodynamic disturbances (absent or reversed end-diastolic flow) were found in 28.1% of C1 and 34.4% of C2; one case of reversed flow was recorded in C2. Although the difference was not statistically significant ($p>0.05$),

a trend toward more severe hemodynamic impairment was noted in C2. In both groups, Doppler abnormalities predominantly emerged in the third trimester.

Abnormalities of the amniotic fluid index were sporadic, with similar frequencies of polyhydramnios and oligohydramnios in both groups ($p>0.05$). Most women had normal amniotic fluid volumes.

Fetal growth restriction was more frequently diagnosed in C2: 2 cases (6.25%) in C1 versus 5 cases (15.6%) in C2.

Most women in both groups delivered at term, although the mean gestational age at delivery was significantly higher in C1: 38.5 ± 1.1 weeks (median 39 weeks) versus 37.97 ± 1.2 weeks (median 38 weeks) in C2 ($p<0.05$). Preterm delivery (<37 weeks) occurred in 6.25% of C2, whereas in C1 pregnancies typically concluded between 38 and 40 weeks.

Vaginal delivery predominated, though the rate of cesarean section was higher in C2 (40.6% vs. 21.9% in C1). Despite the lack of statistical significance ($p>0.05$), the structure of indications differed. In C1, the leading indication was previous uterine scar (4 cases, 57.1%), primarily requiring planned procedures. In C2, indications were more heterogeneous, including maternal factors (uterine scar 7.7%, clinically narrow pelvis 7.7%) and fetal factors (breech presentation 30.8%, fetal distress in the first stage of labor 15.4%, signs of fetal hypoxia 7.7%, placental abruption 7.7%).

Among women delivering vaginally, the overall frequency of intrapartum complications was moderate and similar between groups ($p>0.05$). In C1, the most common complications were fetal distress in the first (4.0%) and second stages (4.0%), labor abnormalities (4.0%), and shoulder dystocia (4.0%). In C2, fetal distress in the first stage (10.5%), placental abruption (5.3%), and clinically narrow pelvis (5.3%) predominated.

Conclusions

1. The findings of this study indicate a high prevalence of extragenital pathology (84.36%) among pregnant women at high risk for hypertensive disorders, with metabolic disorders, somatoform autonomic dysfunction, and varicose disease being the most common. This pattern reflects the typical polymorbidity observed in high-risk populations for hypertensive disorders of pregnancy.

2. Combined prophylaxis with L-arginine and a micronutrient complex was associated with a lower incidence of hypertensive disorders of pregnancy – 15.6% compared to 37.5% in the group receiving standard prophylaxis – and with the absence of severe preeclampsia.

3. Indicators of fetal well-being demonstrated a trend toward better hemodynamic compensation in the combined prophylaxis group, with fewer cases of severe blood flow abnormalities and a lower frequency of fetal growth restriction.

4. Obstetric outcomes were more favorable in the group of pregnant women receiving combined prophylaxis, which contributed to a reduction in the rate of emergency cesarean delivery.

References

1. Dimitriadis, E., Rolnik, D. L., Zhou, W., Estrada-Gutierrez, G., Koga, K., Francisco, R. P. V., et al. (2023). Pre-eclampsia. Nature Reviews Disease Primers, 9(1), 8. https://doi.org/10.1038/s41572-023-00417-6

2. Burton, G. J., Redman, C. W., Roberts, J. M., & Moffett, A. (2019). Pre-eclampsia: Pathophysiology and clinical implications. BMJ, 366, l2381. https://doi.org/10.1136/bmj.l2381

3. Rana, S., Lemoine, E., Granger, J. P., & Karumanchi, S. A. (2019). Preeclampsia: Pathophysiology, challenges, and perspectives. Circulation Research, 124(7), 1094-1112. https://doi.org/10.1161/CIRCRESAHA.118.313276

4. Granger, D. N., & Kvietys, P. R. (2015). Reperfusion injury and reactive oxygen species: The evolution of a concept. Redox Biology, 6, 524-551. https://doi.org/10.1016/j.redox.2015.08.020

5. Joo, E. H., Kim, Y. R., Kim, N., Jung, J. E., Han, S. H., & Cho, H. Y. (2021). Effect of endogenic and exogenic oxidative stress triggers on adverse pregnancy outcomes: Preeclampsia, fetal growth restriction, gestational diabetes mellitus and preterm birth. International Journal of Molecular Sciences, 22(18), 10122. https://doi.org/10.3390/ijms221810122

6. Jovandaric, M. Z., Babic, S., Raus, M., & Medjo, B. (2023). The importance of metabolic and environmental factors in the occurrence of oxidative stress during pregnancy. International Journal of Molecular Sciences, 24(15), 11964. https://doi.org/10.3390/ijms241511964

Makama, M., Nyan, M., Adeyemi, A., Olayemi, O., Balogun, S., Bello, B., et al. (2025). L-Arginine and L-Citrulline for prevention and treatment of hypertensive disorders of pregnancy: Systematic review and meta-analysis of randomized controlled trials. BJOG: An International Journal of Obstetrics & Gynaecology, 132(2), 199-211. https://doi.org/10.1111/1471-0528.17854