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Study of Homocysteine Levels in Women with Congenital Defects and a History of Non-Progression

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Annotation: Reducing maternal and infant morbidity and mortality remains a major medical and social priority, with the prevention of pregnancy complications and fetal malformations representing a key strategy for achieving this goal. Disturbances in folate metabolism and elevated homocysteine levels are recognized risk factors for adverse pregnancy outcomes, including congenital malformations and early reproductive losses. This study aimed to assess homocysteine levels in women with a history of congenital fetal malformations and nonviable pregnancies and to evaluate the effectiveness of L-methylfolate and vitamin B12 supplementation. A total of 155 women with complicated obstetric and perinatal histories were included in the study. Patients in the main groups received L-methylfolate at a dose of 800 µg/day and vitamin B12 (cyanocobalamin) at a dose of 18 µg/day from the preconception period through pregnancy. Homocysteine levels were measured before treatment and dynamically during therapy.

Keywords: homocysteine, L-methylfolate, folic acid, vitamin B12, pregnancy complications, congenital malformations, MTHFR polymorphism, preconception care, folate metabolism.

Introduction

Reducing maternal and infant morbidity and mortality remains a key goal in modern obstetric practice. A significant proportion of adverse pregnancy outcomes, including congenital malformations (CMs) and nonviable pregnancies, are associated with disturbances in the folate cycle and homocysteine metabolism.

Homocysteine is a sulfur-containing amino acid whose levels are regulated by enzymes of the folate and methionine cycles, with the participation of vitamins B6, B12, and folate. Deficiencies of these factors, as well as the presence of genetic polymorphisms, primarily MTHFR, lead to hyperhomocysteinemia (HH). HH is associated with an increased risk of thrombosis, impaired placental blood flow, preeclampsia, fetal growth restriction, spontaneous miscarriages, and neural tube defects [1, 2, 6].

The impact of folates on pregnancy outcomes has been demonstrated in numerous studies. Both synthetic folic acid and L-methylfolate have been shown to effectively increase plasma and red blood cell folate levels and reduce homocysteine concentrations [3,5,7]. Prescribing active forms of folate is especially important for patients with MTHFR gene polymorphisms, who have reduced metabolism of synthetic folic acid.

Despite numerous studies, data on the Uzbek population remains limited. Studying homocysteine levels in women with fetal malformations and nonviable pregnancies will improve diagnosis, prevention, and a personalized approach to managing this high-risk group.

Purpose of the study. To study homocysteine levels in women with a history of congenital malformations and non-viable pregnancies, and to evaluate the effect of methylfolate and vitamin B12 therapy on its dynamics.

Materials and methods

The study included 155 Uzbek women undergoing follow-up at the TMA obstetrics and gynecology center. All participants provided voluntary informed consent.

Formation of groups: Group 1 (n=40) - women with a history of congenital malformations. Group 2 (n=70) - women with a history of non-viable pregnancies. Control group (n=75) - women without a complicated obstetric history.

A study was conducted to determine the distribution of alleles and genotypes of the MTHFR gene (Glu429Ala). The GenePop program was used to test for compliance with the Hardy–Weinberg law.

All patients in the main group were prescribed the following therapy: L-methylfolate 800 mcg/day, cyanocobalamin (vitamin B12) 18 mcg/day, starting from the planning stage until the end of pregnancy.

If necessary, anticoagulants or antiplatelet agents were prescribed in consultation with a hematologist under the supervision of a hemostasiogram. Homocysteine levels were measured before and after treatment.

Results and Discussions

Vitamins B1, B6, and B12, as well as folic acid, are responsible for methionine metabolism. A deficiency of even one of these components can lead to hyperhomocysteinemia. Hyperhomocysteinemia, which occurs due to elevated methionine levels in the blood, can cause fetal malformations. In our study, we found that homocysteine levels were 3.1 times higher in the first group of subjects compared to the control group. This level may have been a trigger for the development of fetal malformations, leading to serious problems for the child. In the second group, this level was 2.5 times higher than in the control group (Table 1). Therefore, the diagnosed hyperhomocysteinemia may have triggered thrombosis in blood vessels. This led to generalized vascular pathology during pregnancy, the development of non-viable pregnancy, and hypertensive disorders.

Table 1. Homocysteine levels in the examined women

Groups	Homocysteine level	
	before treatment	after treatment
Group 1 (n=40)	23.3±0.48	9.5±0.35
Group 2 (n=70)	18.3±0.44	8.4±0.22
Control group, (n=75)	7.5±0.28	

Reducing maternal and infant morbidity and mortality is a priority medical and social task, and the primary means of achieving this is the prevention of pregnancy complications and fetal malformations. Folates are currently widely used as single-ingredient preparations, in vitamin supplements, and even in oral contraceptives. Two forms of the vitamin are used: synthetic FC and L-methylfolate. Synthetic FC (referred to as FC in product labels) is a proven method of folate supplementation. Upon entering the body, FC undergoes a series of enzymatic reactions, resulting in the formation of both depot and active forms. Intake of synthetic FC is directly correlated with increased folate levels in blood plasma and red blood cells and inversely correlated with homocysteine levels. All major studies of efficacy and safety have been conducted on synthetic FC; toxic effects of FC have not been described.

Women in both groups, all with a history of complicated obstetrics, gynecology, and perinatal complications, were prescribed 800 mcg of methylfolate and 18 mcg of vitamin B12 (cyanocobalamin) daily, beginning with pregnancy planning and continuing throughout the remainder of their pregnancy. Treatment was administered in consultation with a hematologist (anticoagulants and antiplatelet agents were prescribed as needed, according to protocol, and monitored by a hemostasis monitor). After prescribing 800 mg of methylfolate, homocysteine levels were monitored. We found a significant reduction in this blood level in both groups (1.9-fold and 1.75-fold, respectively) compared to the control group.

Conclusion

Women with a complicated obstetric history (congenital malformations, nonviable pregnancy) showed pronounced hyperhomocysteinemia, exceeding the control group by 2.5–3.1 times, confirming the pathogenetic role of homocysteine in embryogenesis disorders and early reproductive losses. Administration of 800 mcg of L-methylfolate and 18 mcg of vitamin B12 per day significantly reduced homocysteine levels to levels comparable to the control group. The use of active folates is an effective preventive measure in high-risk women, especially those with MTHFR gene polymorphisms. These data confirm the need for mandatory homocysteine assessment and folate status correction during preconception care and early pregnancy.

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