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RESEARCH ARTICLE

The Role of Elevated Homocysteine Levels in The Risk of Cerebrovascular Events

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Abstract: Hyperhomocysteinemia is considered a potentially modifiable risk factor for cerebrovascular pathology. The aim of this study was to assess the impact of elevated homocysteine levels on the risk of cerebrovascular events in patients with cardiovascular risk factors. A total of 80 patients aged 45–75 years were examined. Plasma homocysteine levels were measured, and neuroimaging, lipid profile analysis, and coagulation studies were performed. Patients were divided into groups with normal homocysteine levels (<15 μmol/L) and hyperhomocysteinemia (≥15 μmol/L). Elevated homocysteine levels were significantly associated with an increased incidence of ischemic stroke and transient ischemic attack, as well as more pronounced cerebrovascular changes. These findings confirm that hyperhomocysteinemia is an independent risk factor for cerebrovascular events and warrants early diagnosis and intervention.

Key words: Homocysteine, ischemic stroke, transient ischemic attack, vascular risk, hyperhomocysteinemia.

INTRODUCTION

Cerebrovascular accidents remain one of the leading causes of mortality and long-term disability worldwide. According to the World Health Organization, stroke ranks second among the causes of death and represents a significant medical and social burden, leading to high rates of disability and a substantial decline in patients' quality of life. In recent years, increasing attention has been paid to the study of modifiable biochemical risk factors of cerebrovascular pathology.

Homocysteine is a sulfur-containing amino acid formed during the metabolism of methionine. Elevated plasma homocysteine levels (hyperhomocysteinemia) are considered an independent risk factor for atherosclerosis, thrombosis, and endothelial dysfunction. According to data from the Framingham Heart Study, increased homocysteine levels are significantly associated with a higher risk of stroke and other cardiovascular events. The pathogenic effects of homocysteine are mediated through a complex set of interrelated mechanisms, including vascular endothelial damage, increased oxidative stress, activation of thrombus formation processes, and stimulation of vascular smooth muscle cell proliferation. An important role in regulating the level of this amino acid is played by the availability of micronutrients in the body, particularly vitamin B12 (cobalamin). As a cofactor of the enzyme

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methionine synthase, vitamin B12 participates in the remethylation of homocysteine to methionine. Deficiency of cobalamin leads to a metabolic block in this cycle, resulting in excessive accumulation of homocysteine in the systemic circulation and triggering a cascade of vascular damage.

Thus, the combined study of homocysteine levels and vitamin B12 status opens new possibilities for pathogenetically grounded primary and secondary prevention of ischemic brain lesions.

METHODS

The study included 80 patients, of whom 44 (55%) were men and 36 (45%) were women. The age of the participants ranged from 45 to 75 years, with a mean age of 61.3 ± 8.4 years.

The inclusion criteria for the main cohort were:

• verified cardiovascular risk factors (arterial hypertension, type 2 diabetes mellitus, dyslipidemia);

• a history or acute data indicating previous ischemic stroke, transient ischemic attack (TIA), or the presence of clinical manifestations of chronic cerebral ischemia.

Examination protocol. A comprehensive examination of patients included laboratory and instrumental diagnostic methods. Laboratory testing involved the determination of total plasma homocysteine levels using an enzyme-linked immunosorbent assay (ELISA). A standard biochemical analysis was also performed, including assessment of lipid profile parameters and indicators of the hemostasis system (coagulogram).

To assess the condition of cerebral structures and the vascular bed, neuroimaging and functional diagnostic methods were used: Magnetic resonance imaging (MRI) of the brain was performed to evaluate the degree of white matter damage and to detect focal lesions.

Ultrasound examination of the brachiocephalic arteries was conducted to assess the degree of atherosclerotic involvement and the presence of hemodynamically significant stenosis.

Depending on the concentration of homocysteine in blood plasma, the patients were divided into two comparable groups:

Group	Number of patients (n)	Homocysteine level (μmol/L)
Group I (normal/borderline level)	38	<15
Group II (hyperhomocysteinemia)	42	≥15

Statistical Data Analysis. The statistical analysis of the results was performed using a software package for biomedical research. The normality of the distribution of quantitative variables was assessed using the Kolmogorov–Smirnov test. Comparisons of quantitative indicators between groups were conducted using the Student's t-test. Associations between qualitative variables were evaluated using the chi-square test (χ^2). To identify predictors of vascular complications, logistic regression analysis was applied. Differences were considered statistically significant at $p < 0.05$.

RESULTS

Comparative analysis of clinical and laboratory parameters revealed a significant difference in total plasma homocysteine levels between the study groups. In Group I (control), the mean concentration was 11.2 ± 2.1 μmol/L, whereas in Group II (hyperhomocysteinemia), it reached 19.8 ± 4.6 μmol/L, indicating a pronounced metabolic imbalance in the patients of the main group.

Analysis of cerebrovascular event frequency showed a significant association between elevated homocysteine levels and the risk of acute conditions. Ischemic stroke, either in history or during the acute period, was

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diagnosed in 52.4% (n = 22) of patients in Group II, more than twice the rate observed in the group with normal homocysteine levels (23.6%, n = 9; p < 0.05). A similar trend was observed for transient ischemic attacks (TIA): their frequency in Group II was 33.3% (n = 14) versus 15.8% (n = 6) in Group I (p < 0.05).

Neuroimaging and ultrasound data deserve particular attention. Patients with hyperhomocysteinemia more frequently showed signs of cerebral microangiopathy: leukoaraiosis on MRI was observed in 69.0% (n = 29) of Group II, compared to only 31.5% (n = 12; p < 0.01) in Group I. Furthermore, elevated homocysteine levels were associated with more severe involvement of major cerebral vessels. Stenotic atherosclerosis of the brachiocephalic arteries (BCA) with luminal narrowing >50% was significantly more frequent in Group II (47%, n = 20) compared to the control group (21%, n = 8; p < 0.05).

To assess the impact of hyperhomocysteinemia on the likelihood of vascular events, a multivariate logistic regression analysis was performed. The results indicated that elevated homocysteine levels serve as an independent predictor of ischemic stroke, increasing the risk by 2.3 times (OR = 2.3; 95% CI 1.4–3.8).

Table 1.

Comparative Characteristics of Clinical and Instrumental Parameters in the Study Groups

Parameter	Group I, normal (n = 38)	Group II, Hyperhomocysteinemia (n = 42)	p
Ischemic stroke, n (%)	9 (23,6%)	22 (52,4%)	<0,05
Transient ischemic attack (TIA), n (%)	6 (15,8%)	14 (33,3%)	<0,05
Leukoaraiosis (MRI), n (%)	12 (31,5%)	29 (69,0%)	<0,01
BCA stenosis >50%, n (%)	8 (21,0%)	20 (47,6%)	<0,05

DISCUSSION

The results of this study indicate that hyperhomocysteinemia (HHC) is an independent and clinically significant predictor of cerebrovascular events. Analysis revealed a clear correlation between elevated plasma homocysteine levels and the frequency of both acute cerebrovascular disorders (ischemic stroke, TIA) and subclinical white matter damage. These findings are consistent with the results of major international prospective studies, including the Framingham Heart Study, which demonstrated a linear relationship between homocysteine concentration and the risk of vascular events.

The pathophysiological mechanism underlying this association is due to the multifaceted effects of homocysteine on the vascular system. A key role is played by the initiation of endothelial dysfunction, stimulation of oxidative stress, and proliferation of vascular smooth muscle cells, which collectively accelerate the process of stenotic atherosclerosis.

Of particular interest is the potential for therapeutic modification of this risk factor. The use of folic acid and B vitamins (B6, B12) effectively reduces homocysteine levels, offering promising opportunities for both primary and secondary prevention of strokes in patients with disturbances in the methionine cycle.

CONCLUSIONS

The present study confirms that elevated homocysteine levels (≥15 μmol/L) are a statistically significant factor increasing the risk of ischemic stroke and transient ischemic attacks. In addition to acute cerebrovascular events, hyperhomocysteinemia is closely associated with the severity of leukoaraiosis and the progression of stenotic atherosclerosis of the major cerebral arteries.

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Given these findings, measuring plasma homocysteine concentrations appears to be a useful component of the diagnostic algorithm for patients at high vascular risk. Timely detection and early correction of metabolic disturbances through vitamin supplementation are essential steps for reducing the likelihood of severe cerebrovascular complications and slowing structural brain tissue degeneration.

REFERENCES

1. Homocysteine Studies Collaboration. Homocysteine and risk of ischemic heart disease and stroke: a meta-analysis. BMJ. 2002.
2. Hankey G.J., Eikelboom J.W. Homocysteine and stroke. Lancet. 2005.
3. Framingham Heart Study. Study data on homocysteine and cardiovascular risk.
4. Wald D.S., Law M., Morris J.K. Homocysteine and cardiovascular disease: evidence on causality. BMJ. 2002.