DOI https://doi.org/10.30525/978-9934-26-655-3-14

HYPERHOMOCYSTEINEMIA, ITS CORRECTION AND ASSOCIATED DISORDERS IN PATIENTS UNDERGOING MAINTENANCE HEMODIALYSIS

ГІПЕРГОМОЦИСТЕЇНЕМІЯ, КОРЕКЦІЯ ЇЇ ТА ПОВ'ЯЗАНИХ З НЕЮ ПОРУШЕНЬ У ПАЦІЄНТІВ, ЩО ЗНАХОДЯТЬСЯ НА ПРОГРАМНОМУ ГЕМОДІАЛІЗІ

Postovitenko K. P.
Candidate of Medical Sciences, Associate Professor, Associate Professor at the Department of Physical and Rehabilitation Medicine National Pyrogov Memorial Medical University Vinnytsia, Ukraine

Постовітенко К. П.
кандидат медичних наук, доцентка, доцентка кафедри фізичної та реабілітаційної медицини Вінницький національний медичний університет імені М. І. Пирогова м. Вінниця, Україна

Iliuk I. A.
Candidate of Medical Sciences, Associate Professor, Associate Professor at the Department of Internal Medcine № 2 National Pyrogov Memorial Medical University Vinnytsia, Ukraine

Ільюк І. А.
кандидат медичних наук, доцентка, доцентка кафедри внутрішньої медицини №2 Вінницький національний медичний університет імені М. І. Пирогова м. Вінниця, Україна

Baranova I. V.
Candidate of Medical Sciences, Associate Professor, Associate Professor at the Department of Physical and Rehabilitation Medicine National Pyrogov Memorial Medical University Vinnytsia, Ukraine

Баранова І. В.
кандидат медичних наук, доцентка, доцентка кафедри фізичної та реабілітаційної медицини Вінницький національний медичний університет імені М. І. Пирогова м. Вінниця, Україна

Introductio. It is well established that patients with chronic kidney disease (CKD) have a markedly increased risk of the development and progression of cardiovascular disease [1, p. 233]. However, the combined impact of hyperhomocysteinemia, folate status, dyslipidemia, and oxidative stress on the progression of cardiovascular pathology in chronic renal failure (CRF), as well as the potential for correcting these abnormalities with high-dose folic acid, remains insufficiently investigated [2, p. 534; 3, p. 488]

Aim: To evaluate the effect of folic acid administration (6 mg daily for 8 weeks) on plasma total homocysteine (tHcy) levels, lipid profile parameters, oxidative stress markers, and cardiovascular status in patients with end-stage renal disease (ESRD) receiving maintenance hemodialysis.

Materials and Methods: A total of 35 patients with stage IV CRF undergoing treatment in a hemodialysis unit were examined. The mean age of the cohort was 37.8 ± 2.53 years. In 23 patients, ESRD developed as a complication of chronic glomerulonephritis, and in 12 patients as a consequence of chronic pyelonephritis. The mean duration of maintenance hemodialysis was 28.3 ± 1.5 months. Patients received folic acid orally at a dose of 6 mg daily for 8 weeks. Plasma total homocysteine levels, vitamin status (serum folate), lipid profile (total cholesterol, HDL cholesterol, LDL cholesterol, and triglycerides), and oxidative stress markers (malondialdehyde (MDA) and carbonyl groups (CG) were assessed at baseline and after 4 and 8 weeks of therapy. Instrumental investigations (echocardiography and assessment of endothelial dysfunction) were performed prior to follow-up blood sampling. Endothelial function was evaluated only in patients with an intact brachial artery.

Between-group differences were analyzed using the nonparametric Mann–Whitney U test. Pearson's correlation analysis was applied to assess associations between variables. Fisher's exact test was used to compare frequencies. Differences were considered statistically significant at $p < 0.05$.

Results: A significant inverse correlation between plasma homocysteine and folate concentrations was observed ($t = 2.77$). After 4 weeks of folate therapy, tHcy levels decreased by 1.5 μmol/L; however, this reduction was not statistically significant ($p > 0.05$), whereas the increase in serum folate by 1.5 μg/L was significant ($p < 0.05$), with a significant negative correlation between these parameters ($r = –0.45$, $p < 0.05$). After 8 weeks of treatment, the reduction in tHcy to 21.9 μmol/L (–19.7%) became statistically significant. An individual decrease in tHcy of ≥5 μmol/L was observed in 11 patients (50%), and an overall reduction in tHcy was documented in 16 patients (72.7%). Folic acid therapy did not produce significant changes in lipid parameters at either 4 or 8 weeks. No significant correlations were found between lipid levels and homocysteine concentrations (all $p > 0.05$). Thus, no significant associations were identified between lipid metabolism parameters on the one hand and folate status or homocysteine levels on the other. During the observation period, a reduction in oxidative stress markers was noted at both 4 and 8 weeks, reaching statistical significance at week 8 ($p < 0.05$). In hemodialysis patients, a direct correlation between tHcy levels and MDA and CG concentrations was detected both before and after folic acid therapy.

Characteristic echocardiographic changes and endothelial dysfunction typical of CRF were identified in dialysis patients and were significantly inversely correlated with homocysteine levels. Endothelial function parameters appeared to be more labile than echocardiographic indices. Severe endothelial dysfunction was observed in dialysis patients. Flow-mediated dilation (FMD) was reduced 6.7-fold compared with healthy individuals and 4.8-fold compared with nephrological patients without renal failure. Endothelium-independent dilation (EID) was reduced 3-fold and 2.6-fold, respectively. Endothelial function indices were more responsive to therapy than echocardiographic parameters. A marked reduction in EID prior to treatment indicated profound endothelial impairment associated with decreased sensitivity to nitric oxide. After 4 weeks of therapy, most endothelial function parameters tended toward normalization, although changes were not statistically significant. After 8 weeks, integral endothelial function parameters improved: FMD increased 2.6-fold and EID 1.6-fold, clearly correlating with the reduction in tHcy levels. Before treatment, a normal FMD value was observed in only one patient (5%); after 4 weeks, also in one patient; after 8 weeks, in 5 patients (27%).

According to chi-square analysis, the increase in the number of patients with normal FMD was statistically significant ($\chi^2 = 3.86$; critical value = 3.82). In contrast, the increase in patients with normal EID (from 15% at baseline to 35% and 38% at 4 and 8 weeks, respectively) was not statistically significant ($\chi^2 = 2.39$). Additional statistical analysis confirmed a strong negative correlation only between FMD and EID parameters t values ranging from 2.31 to 3.53), whereas variations in other indices remained within statistical error.

Conclusions:

1. Eight-week folic acid therapy in dialysis patients resulted in a significant increase in plasma folate levels and a significant reduction in homocysteine concentration, without affecting lipid metabolism parameters.

2. Vitamin therapy was associated with significant suppression of oxidative stress, evidenced by decreased concentrations of lipid (MDA) and protein (CG) oxidation products.

3. Folic acid administration led to a marked improvement in brachial artery endothelial function but did not influence echocardiographic parameters.

Bibliography:

1. Наконечна О., Ярмиш Н., Денисенко С., та ін. Сучасні уявлення про гіпергомоцистеїнемію як предиктора патологічних станів. *Актуальні проблеми сучасної медицини: Вісник Української медичної*

стоматологічної академії. 2025. Том *25*, № 1. С. 231–237. https://doi.org/10.31718/2077-1096.25.1.231

2. Shevchuk S.V., Postovitenko K.P., Iliuk I.A. et all. The relationship between homocysteine level and vitamins B12, B9 and B6 status in patients with chronic kidney disease. *Wiad Lek.* 2019. Vol. 72, № 4. P. 532–538. doi: 10.36740/WLek201904105

3. Sowndarya K., Hegde A., Pawar N. M. et all. Elevated Homocysteine Levels and Vitamin Deficiencies as Potential Risk Markers for Coronary Artery Disease in Apparently Healthy Adults. *Biomedical and Biotechnology Research Journal. 2024* Vol. 8. P. 487–492.