

Hyperhomocysteinemia-Related Serum Metabolome Alterations not Normalized

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Introduction

Hyperhomocysteinemia (HHCys) is an independent risk factor for various diseases such as cardiovascular diseases, Alzheimer's, and cancers. Folate deficiency is one of the significant reasons for HHCys. However, it is not known whether folate deficiency with HHCys is associated with any serum metabolites.

Objectives

Our objective was to identify the metabolic alterations in people having folate deficiency with HHCys and check whether a short-term folic acid therapy could reverse those metabolic changes.

Methods

The study enrolled 34 participants aged between 18 and 40 years having folate deficiency (15 $\mu\text{mol/L}$) and 21 normal healthy individuals. A short-term intervention of oral folic acid (5 mg/day) was done in the HHCys group for 30

days. Untargeted metabolomics analysis of serum was performed in all study subjects before and after the folic acid treatment. Different univariate methods and the multivariable-adjusted linear regression models were employed to determine an association between homocysteine level and metabolite profile.

Results

Metabolomics analysis data showed that many metabolites involved in the biochemical pathways of lipid metabolisms such as polyunsaturated fatty acids, glycerolipids, and phospholipids were downregulated in the HHCys group. Short-term oral folic acid therapy significantly reduced their serum homocysteine level. However, the metabolic pathway alterations observed in folate-deficient HHCys-condition were unaltered even after the folic acid treatment.

Conclusions

Our study revealed that people who have a folic acid deficiency with HHCys have an altered metabolite profile related to lipid metabolism, which cannot be reversed by short-term folic acid therapy.

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