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CASE REPORT

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Dietary support in hyperhomocysteinemia

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Abstract

The study presents a case of a 70-year-old obese male with hyperhomocysteinemia, hypertension, abnormal glucose tolerance, and a history of stroke. Despite medication, his condition persisted due to dietary factors, including excessive salt, protein, and fat intake, and inadequate intake of vitamins B6 and folic acid. The intervention aimed to reduce homocysteine levels, achieve weight loss, improve metabolic health, and optimize nutrient intake. A reduction diet based on DASH and Mediterranean principles was implemented, emphasizing glycemic index/load education and nutrient-balanced meals. After 3 months, significant improvements were observed: weight loss (3.3 kg), reduced body fat percentage, improved body composition, and biochemical enhancements, including decreased homocysteine levels (3.1 μmol/L), increased plasma levels of vitamins B6, B12, and folic acid, and improved lipid profile and glucose levels. These positive outcomes were achieved solely through dietary changes, highlighting the efficacy of tailored dietary interventions in managing complex health conditions without additional pharmacological treatment. The study underscores the importance of personalized dietary strategies in holistic health management, emphasizing the potential for significant health improvements through targeted dietary modifications.

Keywords: case reports, hyperhomocysteinemia, DASH diet, hypertension, dietary management

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Introduction

Homocysteine (Hcy) is produced during physiological processes and is not supplied to the body with food. Hcy is produced in all cells of the human body and is biosynthesized from methionine in multiple steps [1]. It is detoxified primarily in the kidney and liver via the remethylation and transsulfuration pathways. In the skin and blood vessel cells, Hcy, due to the lack of expression of transulfuration enzymes, is only metabolized via the remethylation pathway. In this case, folic acid, which determines the removal of Hcy, plays a key role. Homocysteine serves as a key intermediate compound in methylation reactions. It is synthesized from methionine and then passes through one of two main metabolic pathways: remethylation to methionine, which requires folic acid and vitamin B12 (or betaine in an alternative reaction), and transsulfuration to cystathionine, which requires pyridoxal phosphate (the active form of vitamin B6). These two pathways are coordinated by S-adenosylmethionine [2]. Remethylation is a reversible process and is exacerbated in states of methionine deficiency and low S-adenosylmethionine concentration. It can occur via two pathways. The first involves the conversion of Hcy to methionine, using vitamin B12 (methylcobalamin) as a cofactor.

The presence of folic acid is critically required here, which acts as a methyl group donor. Food-derived folate is then converted to the active form of tetrahydrofolate (THF). In the presence of methylenetetrahydrofolate reductase (MTHFR), 5,10-methylenetetrahydrofolate is formed, then reduced to 5-methylenetetrahydrofolate. This pathway of Hcy metabolism represents the only possibility in arterial endothelial cells, which explains

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the importance of folic acid for vascular physiology. The optimal total Hcy (tHcy) level according to many researchers should be < 10 μmol/L [3]. The upper limits of plasma homocysteine concentration are not clear. It is known that each 5 μmol/L increase in homocysteine increases the risk of coronary heart disease by 20%, regardless of traditional risk factors for coronary heart disease [3–5]. Elevated plasma Hcy levels have a multifactorial basis based on genetic and environmental elements, which can be further subdivided into modifiable factors such as drugs, pregnancy, diet, stimulants, exercise, vegetarian diet and non-modifiable factors e.g.: gender, age, comorbidities, genetic mutations of Hcy metabolizing enzymes, menopause [6, 7].

Severe hyperhomocysteinemia (HHcy) is caused by genetic defects due to congenital deficiency of the enzyme CBS, resulting in homocystinuria and vitamin B12 deficiency. Many drugs are associated with acquired HHcy. These include methotrexate, theophylline, phenytoin, cyclosporine, cholestyramine, metformin, niacin, proton pump inhibitors (e.g., omeprazole), oral contraceptives (OCPs), nicotinic acid (niacin), fibric acid derivatives, sulfasalazine, fenofibrate, L-DOPA, diuretics [6].

Hyperhomocysteinemia can be caused by diseases in which vitamin B12 and B6 and folic acid deficiencies have been identified, e.g., pernicious anemia [8]. HHcy predominantly affects the cardiovascular system and many other pathologies. A consequence of high homocysteine levels is its toxic effects on the cells lining the blood vessels. Altered endothelial function, correlates with weaker vascular tone, leading to vascular inflammation. HHcy-induced endothelial dysfunction is caused by a reduction in nitric oxide (NO), which is produced by the endothelium and causes vasodilation and an increase in oxidative stress following the generation of reactive oxygen species (ROS). In addition, Hcy changes lipid metabolism, initiating oxidative degradation of endothelial lipids and causing loss of cell membrane function. It also promotes the activation of the transcription factor NF-κB causing the activation of inflammation. High endothelial Hcy concentrations are responsible for increased smooth muscle cell proliferation, which, together with altered normal platelet function, may contribute to the formation of atherosclerotic plaques. Finally, Hcy may induce apoptosis of endothelial cells [9]. Studies in cell cultures and animal models have shown that Hcy impairs the ability of endothelial cells to produce nitric oxide and prostacyclin, which are potent endogenous vasodilators [10]. It should be noted that high homocysteine levels are a predictor of coronary heart disease (CHD) onset and may be a particularly important biomarker and prognostic factor in affected individuals at a younger age [11, 12].

Treatment and prevention of HHcy involves the use of folic acid, vitamin B12 and vitamin B6. Preventively, a folate intake of 400 μg, vitamin B12 of 3 μg and vitamin B6 of 2 mg is recommended. Therapeutically, higher doses are used: 500 μg of folic acid, 6–25 mg of vitamin B6, and 100–600 μg of vitamin B12. The efficacy of such therapy is reported in 90% of patients after 6 weeks. The combined use of folic acid and vitamin B12 is more effective than using them separately. There are reports of benefits of including vitamins B2 and B6 to lower homocysteine levels [13].

A high intake of meat and dairy products and in general an excessive intake of protein can raise Hcy levels by increasing methionine loading [14]. In a vegan diet, too low vitamin B12 intake can also lead to elevated Hcy levels [3]. Obesity and even overweight can further impair folic acid absorption and raise homocysteine levels. Methionine (Met) is an essential amino acid that contains sulfur and is derived from food. It is a precursor to other amino acids that contain sulfur, such as homocysteine, cystathionine, cysteine and taurine. As a major donor of methyl groups, Met plays a key metabolic role in transmethylation reactions, leading to the production of S-adenosyl methionine (SAM), involved in the synthesis of several key metabolites, including creatine, choline, epinephrine and almost all methylation reactions in vivo [15]. In proteins, it has an important antioxidant role, stabilizes protein structure and can act as a regulator by reversing redox reactions [16]. Met is mainly present in animal products such as meat (especially red meat), eggs, dairy products (especially casein) and fish. Its sources are also cruciferous vegetables (broccoli, cauliflower, Brussels sprouts), peas, beans, as well as cereal products, sesame and Brazil nuts. In the context of human nutrition, the dietary requirement for methionine and cysteine is referred to as the total sulfur amino acid requirement.

Material and methods

We present the case of an obese man in his 70s, with low physical activity, diagnosed with hypertension, abnormal tolerance glucose, hyperhomocysteinemia and having suffered an ischemic stroke. The patient's medication interview revealed that he was taking metformin XR, lecarnidipine, potassium chloride, tetrahydrate magnesium hydrogen aspartate and ramipril. It is worth noting that metformin increases blood homocysteine levels and interferes with vitamin B12 absorption. The respondent presented to the clinic for weight reduction and glycemic improvement. Based on the dietary history, there was an excessive intake of salt, protein and fat, an excess of simple sugars and too little fiber. Vitamin

B6 and folic acid intake were below normal and vitamin B12 intake was within normal limits.

The main objectives of the dietary management in this patients were to reduce homocysteine levels, gradually reduce body weight by 10–15%, balance vitamin D3 levels, normalize and improve metabolic health parameters, improve glycemic control, and take care of the satiety index through an adequate supply of protein, fiber and fat. A reduction diet adapted to the recommendations in the aforementioned disease entities was used. The initial calorific value of the reduction diet was set at 1800 kcal and was reduced to 1600 kcal after one month.

A 7-day menu based on the principles of the DASH diet and the Mediterranean diet was drawn up for the patient. Lists of foods containing the most folate, vitamin B12 and vitamin B6 were prepared. In addition, the study participant was provided with a table of foods available in Poland, rich in antioxidants, prepared based on the ORAC scale, and dietary substitutions that allowed the replacement of products in a given food group.

As the patient in the study had abnormal glucose tolerance and multiple co-morbidities, there was a strong emphasis on education regarding glycemic index and glycemic load concepts. The importance of proper meal preparation and the impact of food fineness and degree of processing on the glycemic index was explained. The distribution of the different ingredients on a plate developed by the National Center for Nutrition Education was shown. Values for macronutrients and micronutrients were calculated according to the 2021 standards of the Food and Nutrition Institute. When balancing the diet, special attention was paid to the levels of vitamin B12, folic acid, vitamin B6, vitamin B2 and antioxidant vitamins such as vitamins A, E and D. The levels of individual dietary fatty acids and cholesterol were also important because of the risk of cardiovascular disease resulting from HHcy and co-morbidities and a history of stroke. Standards for fatty acids were developed based on the IOH guidelines and the DASH diet, which is also recommended for hypertension. In addition, the methionine, cysteine and tryptophan content of the diet was assessed. Attention was given to an adequate supply of sodium, magnesium, potassium, calcium, fiber and the calcium/phosphorus ratio (1:1). Cholesterol intake was reduced to 200 mg, total fat intake and fiber supply were increased, simple carbohydrates and sucrose were reduced. The supply of vegetable protein to animal protein was balanced at a ratio of 1:1.

Results

The patient experienced some difficulties in adapting to the dietary recommendations. Despite occasional deviations from the menu, a change of habits was introduced using the small-steps method. Fried meals were successfully replaced by cooking and baking. Meat and cheese consumption was reduced, and vegetables were introduced into each meal. The respondent also introduced daily short walks.

At the end of the 3-month nutritional therapy, significant changes in anthropometric indexes and biochemical markers were noted. Table 1 shows the results of the initial and final measurements.

Conclusions

The nutritional therapy to which the patient has been subjected has had positive effects related to overall health. Body weight was reduced, especially the amount of body fat and also the WHR index. Blood biochemical parameters improved significantly. An increase in the plasma levels of vitamins B6, B12 and folic acid translated into a decrease in homocysteine levels by 3.1 μmol/L. The lipid profile and blood glucose level also improved remarkably. It is noteworthy that the above changes were achieved only by changing the patient's dietary habits, without additional supplementation or pharmacological treatment.

Article information and declarations

Ethics statement: Due to the clinical case presented, which describes the patient's feeding interventions, because this work is a clinical case report that describes the patient's nutritional interventions, this study does not require a formal ethical review due to its retrospective and anonymous nature. Patient data were provided in a way that ensured confidentiality and anonymity. All interventions were carried out by the ethical principles of medical practice and the patient consented to participate in the therapeutic process.

Author contributions: The authors collaborated on all stages of the preparation of this study. Monika Kruszelnicka: collected, analyzed and interpreted the patient's clinical data and conducted an assessment of the effects of nutritional therapy. Also, edited and prepared the content of the article. Katarzyna Kulus: assisted in data analysis, preparation and editing of the article and reviewing the scientific literature. Beata Machnicka: assisted in data analysis and interpretation. Additionally, made important intellectual contributions through consultation and editing of the article. Mariusz Kasprzak: participated in the evaluation

Table 1. Comparison of measurement results at the beginning and end of therapy

Parameter	Value before therapy	Value after therapy	Change in value	Standard value	Unit
Anthropometrics parameters					
Body height	170	170	–	–	cm
Body weight	111.5	108.2	↓ 3.3	–	kg
Waist measurement	131	126	↓ 5	–	cm
Hip measurement	120	117	↓ 3	–	cm
Waist to hip ratio (WHR)	1.09	1.08	↓ 0.01	< 1	–
Body fat percentage	36.1	32.9	↓ 3.2	15–20	%
Fat	40.3	36.7	↓ 3.6	9.5–13.9	kg
Visceral fat level	20	18	↓ 2	1–9	–
Body water content	51.3	51.5	↑ 0.2	36.6–38.9	kg
Muscle mass	64.9	65.4	↑ 0.5	47.1–50.2	kg
Lean body mass	71.2	71.5	↑ 0.3	50.9–54.1	kg
Biochemistry parameters					
Homocysteine	25.9	22.8	↓ 3.1	4.5–12.4	μmol/L
Vitamin B_6	13.4	14.3	↑ 0.9	8.7–27.4	μg/L
Vitamin B_{12}	388	417	↑ 29	191–771	pg/mL
Folic acid	6.8	10.3	↑ 3.5	3.89–26.8	ng/mL
Hemoglobin	16.3	16.8	↑ 0.5	12–18	g/dL
Total cholesterol	211	172	↓ 39	115–190	mg/dL
HDL	44	51	↑ 7	> 40	mg/dl
LDL	135	105	↓ 30	< 115	mg/dl
Glucose	119	101	↓ 118	70–99	mg/dl
CRP	< 1	< 2	↑ 1	< 10	–

of treatment effects and contributed through consultation on scientific and ethical standards.

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Conflict of interest: The authors declare that they have no conflicts of interest related to the content of this article.

Supplementary material: No supplementary material is attached to this article. All relevant information can be found in the main content.

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