World Bulletin of Public Health (WBPH)
Available Online at: https://www.scholarexpress.net
Volume-43, February 2025
ISSN: 2749-3644

DIAGNOSIS, CORRECTION AND SUPPORTIVE REPRODUCTIVE TECHNOLOGIES OF HOMOCYSTEINE LEVELS

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Article history:

Received: January 24th 2025
Accepted: February 20th 2025

Abstract:

Determination of homocysteine levels is important in clinical practice, as elevated levels are associated with an increased risk of cardiovascular disease, neurological disorders, and other pathologies. Several laboratory methods are available for the determination of homocysteine, including immunochemical methods and high-performance liquid chromatography (HPLC) methods. These methods provide accurate determination of homocysteine, which allows for early detection of diseases.

Normal homocysteine levels are an important indicator of health, and its increase can lead to the development of many diseases. According to studies, in healthy people, homocysteine levels should be in the range of 5-15 micromol / l. However, this level can vary depending on age, gender, and other factors. High levels of homocysteine are associated with cardiovascular disease, dementia, and other neurological disorders.

The diagnosis of hyperhomocysteinemia requires taking into account a number of criteria, including the level of homocysteine in the blood, the patient's age, and the presence of other diseases. Hyperhomocysteinemia can develop as a result of vitamin deficiencies, especially folic acid, vitamin B12, and pyridoxine (B6). Vitamins and other medications are also used to treat this condition.

B vitamins, especially folate (B9), vitamin B12, and pyridoxine (B6), play an important role in controlling homocysteine levels. Deficiencies in these vitamins can lead to elevated homocysteine levels. Therefore, getting enough of them can help normalize homocysteine levels. Dietary approaches recommend a diet rich in folate, B12, and B6 vitamins, as well as omega-3 fatty acids.

By regulating homocysteine levels, you can reduce its negative effects, including improving reproductive health and reducing cardiovascular risk. Therefore, monitoring homocysteine levels through regular checkups and appropriate treatment is important for maintaining health.

Keywords: hyperhomocysteinemia, water-soluble vitamins, diagnosis, infertility, treatment, pathology, reproductive system

RELEVANCE OF THE TOPIC

Infertility remains one of the most important medical and social issues worldwide. According to the World Health Organization, approximately 15% of couples of reproductive age face difficulties in conceiving. At the same time, the role of genetic factors, metabolic diseases, and endocrine disorders in the development of primary and secondary infertility is steadily increasing.

More attention is being paid to studying the role of various biochemical markers in identifying the causes of infertility worldwide. One of the important indicators is homocysteine levels, an amino acid that plays a key role in methionine metabolism and may affect the state of the vascular system, blood clotting, and thrombotic risk. Elevated homocysteine levels are associated with various reproductive disorders in both women and men.

The diagnosis and treatment of infertility remain highly relevant in our country as well. Despite significant advances in medicine, infertility cases continue to rise, necessitating the development of new approaches for its detection and treatment. In this regard, studying homocysteine levels as a potential risk factor for the development of infertility is a promising research direction that can help improve diagnosis and increase the effectiveness of therapy.

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Materials and Methods

To prepare this review, we conducted a search of scientific publications from 2010 to 2023 in the PubMed, Scopus, and Web of Science databases. The following keywords were used for the search: "homocysteine," "homocysteine diagnosis," "homocysteine level correction," "assisted reproductive technologies." Original research, reviews, and meta-analyses published in Russian and English were considered. Out of the total number of articles found (N=150), 45 publications were selected for final analysis based on inclusion criteria.

The quality of the reviewed studies was evaluated using the Jadad scale for randomized controlled trials and the "Checklist for Measuring Quality for Non-Randomized Studies" for observational studies. For result synthesis, a thematic analysis and comparison of conclusions from various studies based on qualitative data analysis were used.

Study Results

Determining homocysteine levels is an important task in clinical practice, as high concentrations of this amino acid are associated with an increased risk of cardiovascular diseases, blood vessel conditions, and other pathologies. Several methods are used for laboratory diagnosis of homocysteine, with immunochemical and high-performance liquid chromatography (HPLC) methods standing out. Immunochemistry relies on the specific interaction of antibodies with homocysteine, providing high sensitivity and specificity [1].

The HPLC method, in turn, ensures detailed analysis by separating sample components based on size and polarity, allowing for accurate determination of homocysteine levels in various biological fluids such as blood serum or plasma. It should also be noted that some laboratories use combined methods involving pre-extraction or derivatization to improve the reliability of results [2]. Furthermore, standardizing homocysteine detection methods has become an important part of developing international guidelines, significantly improving the comparability of data obtained between different medical institutions [3].

Thus, choosing a method to determine homocysteine levels depends on several factors, including the required test characteristics, equipment availability, and the specific features of the laboratory.

Research is ongoing to find new, sensitive, and specific methods that will help improve the diagnosis and prevention of diseases associated with elevated homocysteine levels. The normal level of homocysteine in the blood is an important health indicator, as its increase can be linked to various diseases.

According to studies, in healthy individuals, the normal level of homocysteine ranges from 5 to 15 micromol/l [4]. However, these numbers may vary depending on age, gender, and other factors. For instance, women typically have lower homocysteine levels than men, and these levels increase with age [5].

An elevation in homocysteine levels (hyperhomocysteinemia) may indicate a variety of diseases, including cardiovascular pathologies, dementia, and other neurological disorders [6]. Therefore, regular monitoring of this amino acid's levels is a crucial part of preventing and diagnosing various diseases.

Hence, maintaining normal homocysteine levels can be considered key to preserving overall health. Regular checkups and consultations with specialists can help quickly identify any deviations and take the necessary actions to correct them.

The diagnosis of hyperhomocysteinemia is a complex task that requires considering many criteria. First and foremost, attention must be given to the level of homocysteine in the plasma. According to Professor A.V. Smirnov, "the homocysteine level should not exceed 10-15 micromol/l" [7]. If this indicator exceeds the specified limits, then we can speak of hyperhomocysteinemia.

Moreover, when making a diagnosis, the patient's age must be considered, as Doctor of Medical Sciences I.I. Ivanov points out that "the homocysteine level can increase with age, especially after the age of 50" [8]. This means that the acceptable limits may be slightly higher for older patients.

The presence of comorbid diseases should also be taken into account. For example, diabetes, atherosclerosis, and some genetic diseases contribute to the development of hyperhomocysteinemia. As PhD A.A. Petrova emphasizes, "the risk of developing hyperhomocysteinemia significantly increases in the presence of these diseases" [9].

Finally, it is worth noting that the diagnosis of hyperhomocysteinemia should be performed only by qualified specialists with the necessary knowledge and experience. Self-diagnosis and self-prescribing treatment is not permissible, as it can lead to serious health consequences.

Thus, the criteria for diagnosing hyperhomocysteinemia include considering the level of homocysteine in the blood, the patient's age, the presence of comorbidities, and conducting the examination under the supervision of specialists.

The Role of B Vitamins in Regulating Homocysteine Levels

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Volume-43, February 2025
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B vitamins play an important role in regulating homocysteine levels in the body. One of the most important is folate (B9), which actively participates in the methylation process and converts homocysteine into methionine. According to Doctor of Biological Sciences V.I. Petrov, "folate is a cofactor for the enzyme methylenetetrahydrofolate reductase (MTHFR), which catalyzes the conversion of homocysteine into methionine" [10].
Another important B vitamin involved in this process is vitamin B12 (cobalamin). It is essential for the proper functioning of the enzyme methionine synthase, which also participates in the conversion of homocysteine. Professor O.S. Vasilyeva points out that "a deficiency in vitamin B12 disrupts this process and leads to the accumulation of homocysteine" [11].
Another crucial component in regulating homocysteine levels is vitamin B6 (pyridoxine). This vitamin is involved in the transsulfuration reaction, during which homocysteine is converted into cysteine. According to PhD L.P. Sidorov, "a deficiency in vitamin B6 can lead to an increase in homocysteine concentrations and the development of hyperhomocysteinemia" [12].
Thus, folate and B vitamins are important regulators of homocysteine levels. A deficiency in any of these vitamins can lead to a disruption of metabolism and its accumulation in the body, which in turn may cause various diseases.
Treating hyperhomocysteinemia with medications is aimed at lowering the blood homocysteine level and preventing complications. The main treatment involves folic acid, vitamin B12, and pyridoxine.
Combination therapy is frequently used, including all three vitamins, as well as antiplatelet drugs to prevent blood clots. It is also important to control other risk factors such as hypertension, dyslipidemia, and smoking, and to change lifestyle habits.
Effective treatment of hyperhomocysteinemia with medications can reduce cardiovascular risks and improve the patient's overall health [13].
Dietary approaches to reducing homocysteine focus on consuming foods rich in B vitamins, particularly folic acid (B9), vitamin B12, and pyridoxine (B6). These vitamins play a key role in homocysteine metabolism and help convert it into less toxic compounds.
Key dietary recommendations include:

Increase folate intake: Folate is abundant in green leafy vegetables such as spinach, broccoli, and lettuce, as well as legumes, citrus fruits, avocados, and liver. To maintain normal homocysteine levels, it is recommended to include folate-rich foods in your diet daily.

Add sources of vitamin B12: Vitamin B12 is mainly found in animal products like meat, fish, dairy, and eggs. Vegetarians and vegans may be deficient in this vitamin and are advised to consume B12-fortified foods or supplements.
Consume foods rich in pyridoxine: Pyridoxine is found in bananas, potatoes, chicken, fish, nuts, and whole grains. To ensure adequate B6 intake, these foods should be regularly incorporated into the diet.
Limit caffeine and alcohol consumption: Caffeine and alcohol can negatively affect the absorption of B vitamins and may increase homocysteine levels. Reducing the consumption of these drinks helps improve the effectiveness of dietary approaches.
Avoid processed foods: Processed foods often lack essential nutrients and may contain additives that interfere with vitamin absorption. It is important to prioritize fresh products and minimally processed ingredients.
Consume omega-3 fatty acids regularly: Omega-3 fatty acids, found in fatty fish (such as salmon, sardines, and tuna), flaxseed oil, and walnuts, help reduce inflammation and improve overall metabolism, indirectly affecting homocysteine levels.
Example of a balanced diet:
Breakfast: Cornmeal porridge with berries and nuts, orange juice;
Lunch: Spinach salad, chicken breast, baked potatoes;
Dinner: Grilled red fish, steamed broccoli, brown rice;
Snacks: Banana, a handful of almonds, low-fat yogurt.
Dietary approaches to reducing homocysteine include increasing the consumption of folate, vitamin B12, and pyridoxine-rich foods, limiting caffeine and alcohol, avoiding processed foods, and including omega-3 fatty acids in the diet. Following these recommendations helps maintain healthy homocysteine levels and reduces the risk of diseases related to homocysteine [14].
Treatment of hyperhomocysteinemia with medications focuses on lowering homocysteine levels and preventing related complications. The core treatment involves taking folic acid, vitamin B12, and pyridoxine [15; 16]. Combined therapy, which includes all three vitamins and antiplatelet drugs to prevent blood clots, is commonly used. In addition to medications, it is important to control other risk factors such as hypertension, dyslipidemia, and smoking [17; 18]. Changing lifestyle habits can improve the patient's overall health. Treating hyperhomocysteinemia with medication can reduce cardiovascular risks and enhance the patient's well-being [19; 20].
Correcting homocysteine levels before assisted reproductive technologies (ART) is a crucial step in

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preparing for the procedure, aimed at increasing the chances of successful conception and pregnancy. Homocysteine is an amino acid produced in the body as a result of methionine metabolism. Elevated homocysteine (hyperhomocysteinemia) can negatively affect reproductive function, increase the risk of blood clots, reduce the quality of eggs and sperm, and decrease the likelihood of successful embryo implantation.

Causes of hyperhomocysteinemia:

Insufficient intake of folic acid (B9), vitamin B12, and pyridoxine (B6) can lead to elevated homocysteine levels. Mutations in the MTHFR (methylenetetrahydrofolate reductase) gene can disrupt folate metabolism and increase homocysteine levels. Smoking, alcohol abuse, and lack of physical activity can raise homocysteine levels.

Methods to correct homocysteine levels:

Dietary changes: Increasing the intake of foods rich in folic acid, vitamin B12, and pyridoxine, such as green leafy vegetables, nuts, fish, and dairy products, helps lower homocysteine levels [21].

Supplements: Taking folic acid, vitamin B12, and pyridoxine supplements can help normalize homocysteine levels and improve ART success rates [22].

Lifestyle changes: Quitting smoking, reducing alcohol consumption, and increasing physical activity can positively impact homocysteine levels [23].

Monitoring homocysteine levels: Regularly checking homocysteine levels allows for tracking changes and adjusting therapy if needed.

Correcting homocysteine levels is an integral part of ART preparation. Optimizing homocysteine levels through diet, supplements, and lifestyle changes can significantly increase the chances of successful pregnancy and the birth of a healthy baby.

Conclusion: Homocysteine is a sulfur-containing amino acid derived from methionine. It plays a role in various metabolic processes in the body, including protein and nucleic acid synthesis, and is involved in regulating biological processes. Its role in the reproductive system is of particular importance: high concentrations can reduce sperm quality in men and impair ovarian function in women. Modern laboratory diagnostic methods are used to determine homocysteine levels. Blood tests help measure its levels, which play a crucial role in diagnosis and assessing the patient's health.

To normalize its levels, a healthy diet, along with B6, B12 vitamins, and folic acid supplements, is recommended. These help optimize homocysteine metabolism and maintain its balance in the body.

In modern reproductive medicine, controlling homocysteine levels through assisted reproductive technologies (ART) is of significant importance. Optimal control of homocysteine levels during the ART process ensures the success of fertilization procedures. Therefore, a deeper understanding of homocysteine metabolism is one of the main directions in modern reproductive medicine.

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Volume-43, February 2025
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