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CONTINUING EDUCATION

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Vitamin B12

Vitamin B12, also known as cobalamin, is a water-soluble vitamin that is derived from animal products such as red meat, shellfish, dairy, and eggs. Fruit and vegetables do not contain vitamin B12. The ability to absorb vitamin B12 from food declines with age.

Intrinsic factor is a glycoprotein produced by parietal cells in the stomach and necessary for the absorption of vitamin B12 in the terminal ileum. Once absorbed, vitamin B12 is used as a cofactor for enzymes that are involved in the synthesis of DNA, fatty acids, and myelin. Vitamin B12 excess is stored in the liver.

Vitamin B12 deficiency is common, and the incidence increases with age. Vitamin B12 deficiency can lead to hematologic and neurological symptoms.

Signs and symptoms

Vitamin B12 deficiency can cause a variety of symptoms, including:

- Fatigue
- Headaches
- Depression
- Pale or yellow skin
- Cognitive impairment
- Pain and inflammation of mouth and tongue
- Paraesthesia in hands and feet
- Vision disturbances
- Impaired coordination or ataxia
- Muscle cramps and weakness

Vitamin B12 deficiency may also contribute to reducing responsiveness to antidepressants.

Neurological impairment in older persons is common with vitamin B12 deficiency. It may present with proprioception and vibration loss due to peripheral sensory neuropathy. Other common neurological findings include:

- Paraesthesia
- Gait ataxia
- Abnormal reflexes
- Bowel/bladder incontinence
- Optic atrophy
- Altered smell and taste
- Lethargy
- Extrapyramidal signs

Autonomic dysfunction can also occur, leading to orthostatic hypotension and syncope. In advanced stages, cognitive decline, psychosis with hallucinations, and depression may be observed.

Evaluation

The Therapeutic Guidelines recommends testing for vitamin B12 concentration every one to two years in people with risk factors for vitamin B12 deficiency.

If supplementation is required, vitamin B12 blood concentration should be rechecked 3 to 6 months after initial supplementation. The dosage and route of supplementation should be adjusted according to response.

Serum potassium concentration should be measured during initiation of vitamin B12 treatment, and hypokalaemia corrected as needed.

Folic acid status should be assessed, as administering folic acid supplements to a person deficient in vitamin B12 without B12 supplementation can lead to an irreversible exacerbation in neurological features.

Pernicious anaemia

The most common, non-dietary cause of vitamin B12 deficiency is pernicious anaemia.

Pernicious anaemia is an autoimmune disorder that affects the gastric mucosa's production of intrinsic factor leading to vitamin B12 deficiency and megaloblastic anaemia. Other causes of megaloblastic anaemia include folic acid deficiency, altered pH in the small intestine, and lack of absorption of vitamin B12 complexes.

Clinical onset of pernicious anaemia usually is usually insidious and vague. The classic triad of weakness, sore tongue, and paraesthesia may be present.

Treatment includes vitamin B12 supplementation, with higher doses needed in people with vitamin B12-associated central nervous system (CNS) impairment.

Food-bound malabsorption

Food-bound cobalamin malabsorption syndrome is characterised by the inability to release vitamin B12 from food or intestinal-binding proteins, generally because of achlorhydria (absence of hydrochloric acid in the gastric secretions). Conditions such as *Helicobacter pylori*-related gastritis, intestinal bacterial overgrowth, Sjogren's syndrome and chronic alcoholism can lead to inadequate digestion of vitamin B12 from food.

Vitamin B12 deficiency commonly occurs with malabsorption syndromes such as Crohn's disease and coeliac disease.

Total or partial gastrectomy can also cause vitamin B12 deficiency. Supplementation is always required after gastric surgery.

Some medications can also determine food-bound cobalamin malabsorption, including:

- Metformin
- Proton pump inhibitors
- H2-receptor antagonists

People with diabetes taking metformin are at a higher risk of developing vitamin B12 deficiency. Proton pump inhibitors (PPIs) such as omeprazole, esomeprazole, pantoprazole, and lansoprazole can also cause vitamin B12 deficiency, especially with higher doses and long-term use.

Protective effect

Vitamin B12 is associated with possible protection against Parkinson's disease, amyotrophic lateral sclerosis (ALS) progression, and fatty liver disease severity.

A recent study found that higher total intake of vitamin B12 was associated with lower risk for Parkinson's disease. Over 13,000 people were followed over 30 years, with around 1000 diagnosed with Parkinson's disease during this period. Participants with higher total intake of vitamin B12 had a 236% lower risk for Parkinson's disease.

In a separate study ultrahigh-dose of methylcobalamin, an active form of vitamin B12 analogue, was found to slow functional decline by 43% in patients with early-stage ALS. The 50mg dose was administered twice-weekly via intramuscular injection for 16 weeks.

Vitamin B12 and folic acid may also play a role in preventing or delaying disease progression in non-alcoholic steatohepatitis (NASH).

Treatment

Treatment of vitamin B12 deficiency involves repletion with B12. In newly diagnosed patients, 1000mcg of B12 is given intramuscularly once a week for two to four weeks to replenish stores before switching to dosing every 2 to 3 months.

Oral vitamin B12 at 1000mcg daily is also effective.

Recommended maintenance therapy includes:

- Cyanocobalamin spray 500 to 1000 micrograms sublingually, daily
- Hydroxocobalamin 1000 micrograms intramuscularly, every 2 to 3 months
- Mecobalamin 1000 micrograms sublingually, daily
- Cyanocobalamin 50 to 200 micrograms orally, daily.

Oral vitamin B12 has similar benefits to IM vitamin B12 and appears as safe. Most adults with vitamin B12 deficiency require lifelong maintenance therapy after initial intramuscular therapy.

Skin and urine may appear red for weeks following administration.

Outcomes

For patients who are promptly treated with vitamin B12, neurological symptoms partially resolve, and the progression may stop. Patients with a long history of neurological symptoms may have residual effects.

Summary

Vitamin B12 (cobalamin) is necessary for basic body functions, such as the growth and development of red blood cells and the nervous system. Vitamin B12 deficiency is very common among people in residential aged care. Many factors contribute to vitamin B12 deficiency, such as age, blood disease, vegetarian diet, indigestion, use of some medications, as well as poor nutrition. Early recognition and treatment of vitamin B12 deficiency is important to mitigate the risk of irreversible neurological impairment. Life-long replacement is usually necessary.

References

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