B VITAMIN GROUP

ENERGY, NERVOUS SYSTEM AND MITOCHONDRIAL SUPPORT

Clinical Summary

B vitamins represent a large group of water-soluble essential micronutrients that play a role in a variety of metabolic and regulatory processes required for human health.[1] They are cofactors used by hundreds of enzymes that carry out essential functions such as energy metabolism, DNA, protein and neurotransmitter synthesis and other critical functions such as red blood cell production, and modulation of inflammation and immunity.[2]

While each B vitamin has an individual mechanism of action, they also have complementary and overlapping functions. Therefore, supplementation with a B complex may help to support a wide range of health conditions including cardiovascular disease, stress and insomnia, cognitive decline, infertility, migraines and many more.

Clinical Guide to Supplementation

Step 1: Assess 'Clinical signs and symptoms of B vitamin deficiency'

Step 2: Establish nutritional and lifestyle risk factors – See 'Clinical Presentations and Risk Factors'

Step 3: Consider evidence-based applications and mechanisms – See 'Clinical Uses and 'Mechanisms of action'

Step 4: Review possible side effects and drug-nutrient interactions – See 'Safety'

Clinical Presentations and Risk Factors

Signs and Symptoms of B Vitamin Deficiency

- Fatigue.[3]
- Memory and cognitive impairment.[4]
- Psychological symptoms such as irritability, anxiety and depression.[5]
- Numbness and tingling in hands and feet.[6]
- Frequent headaches and migraines.[7]
- Cracks around the mouth.[8]
- Anaemia, macrocytic and megaloblastic anaemia.[9]
- High homocysteine levels.[10]

Key Nutrient Considerations

- Vitamin B1 (thiamine)
- Vitamin B2 (riboflavin)
- Vitamin B3 (niacin)
- Vitamin B5 (pantothenic acid)
- Vitamin B6 (pyridoxine)
- Vitamin B7 (biotin)
- Vitamin B9 (folate)
- Vitamin B12 (cobalamin)

Additional Diet and Lifestyle Considerations

- **Pernicious anaemia:** an autoimmune condition, characterised by the presence of anti-intrinsic factor antibodies and often responsible for Vitamin B12 deficiency.[11]
- **Gastrointestinal imbalances:** such as hypochlorhydria, *H. Pylori* infection, small intestinal bacterial overgrowth (SIBO), atrophic gastritis, dysbiosis reduce the absorption of vitamin B12[12] and other B vitamins.[13]
- **Heavy alcohol intake:** misusing alcohol can lead to poor absorption of thiamine and negatively affect the way thiamine is utilised within cells.[14]
- **Genetics:** Individuals with risk variants of the following genes may have reduced capacity to absorb, utilise or transport some of these B vitamins: MTHFR C677T (Vitamin B2 and folate); CBS rs234706 (Vitamin B6); MTRR rs1801394 and FUT2 rs602662 (Vitamin B12).[15,16,17]
- **Pregnancy:** there is an increased need for B vitamins before and during pregnancy.[18,19]
- **Vegetarianism and veganism** increase risk for vitamin B12 deficiency.[20,21]
- **Age:** Deficiencies of Vitamin B6,[22] B12[23] and folate[24] are common in older adults, due to reduced food intake and the ability to absorb these nutrients.

Clinical Uses and Mechanisms

Clinical Uses

1. Prevention of cardiovascular disease and reduction of homocysteine levels: B vitamins, including vitamins B6 and B12 and folate, play vital roles in the metabolism of homocysteine. Deficiency of either of these B vitamins can lead to an elevated circulating level of total homocysteine (tHcy), which has been implicated in the development of cardiovascular disease.[25,26,27,28]

2. Reduction of stress and improvement of overall energy: Vitamin B5 is essential for adrenal cortex function and the synthesis of steroid hormones, and its supplementation may be beneficial in exhaustion.[29] Chronic stress depletes vitamin B6, thus supplementation with B6 could be used as a therapeutic strategy in reducing stress.[30,31] Elevated levels of the stress hormone cortisol appear to suppress levels of folate and B12[32] and stress has been associated with elevated levels of homocysteine.[33]

3. Prevention of cognitive decline: Vitamins B6, folate, and B12 slow cognitive decline in people with mild cognitive impairment, particularly in those with elevated homocysteine levels.[34,35,36]

4. Support in mood and behaviour: Low levels of Vitamin B6,[37] Vitamin B12[38] and folate[39,40] have been associated with higher incidences of depression and other mood disorders. In a clinical trial, a methylated B complex showed improvement in mood symptoms, mental health and quality of life in adults with depression.[41]

5. Blood sugar regulation: Biotin has been shown to significantly reduce HbA1c and fasting blood glucose (FBG).[42] Also, a combination of folic acid and B12 may improve glycaemic control and insulin resistance in people with Type 2 diabetes.[43,44]

6. Prevention and treatment of headaches and migraine attacks: Folate, vitamin B6, and B12 have been shown to be beneficial for the prevention and acute treatment of migraine headaches and tension-type headaches - both in frequency and intensity.[45] The benefits were shown to be greater in those with genetic polymorphisms (carriers of MTHFR C677T and MTRR A66G genes) affecting homocysteine metabolism.[46,47]

7. Pain management: Vitamins B1, B6 and B12 have been shown to have benefits when used as an adjunct to analgesic medications for a number of pain-related disorders.[48,49,50,51,52]

8. Hormonal health and fertility: Folate supplementation is widely used for fertility, for the inhibition of embryonal neural tube defects in pregnancy and is important for lowering homocysteine levels.[53,54,55]

Mechanisms of Action

Reduction of homocysteine levels: Folate and vitamin B2, B6 and B12 are essential for the methylation of homocysteine (HCy) to methionine and thus lowering elevated HCy. Elevated HCy increases the likelihood for oxidative stress, leading to negative events like mitochondrial membrane damage and DNA strand breakage.[56,57,58,59,60]

Enhances mitochondrial function and energy metabolism: Vitamin B1, B2, B3, B5 and Vitamin B12 are involved in ATP synthesis and the metabolism of carbohydrates, fats and proteins.[61,62,63] Vitamin B6 is needed for amino-acid synthesis and helps release stored glucose from the liver and muscles in a process called glycogenolysis.[64]

Supports blood sugar control: Biotin (and chromium) regulates insulin secretion from pancreatic beta cells[42] and regulates glucokinase expression which plays a role in glucose stimulated insulin secretion, post prandial hepatic glucose uptake and the suppression of hepatic glucose output by elevated plasma glucose.[65] Vitamin B6 is an essential cofactor in the Kynureine (KYN) – NAD pathways and its deficiency may interfere with the production, release and biological activity of insulin.[66,67] Therefore, adequate B6 status may help to prevent the development of diabetes in depression and other conditions characterised by stress and inflammation.[68,69]

Supports red blood cell production: Folate and vitamin B12 have crucial roles in erythropoiesis, a process in which red blood cells (RBC) are produced.[70] Deficiency of these nutrients can lead to decreased RBC production and increased mean cell volume (MCV) and subsequently to megaloblastic anaemia.[71,72]

Supports neurotransmitter formation: Vitamin B6 is a coenzyme required for the synthesis of neurotransmitters, serotonin, GABA, dopamine, and norepinephrine.[73] Vitamin B1 is involved in the biosynthesis of acetylcholine and GABA[74] and also required for neurotransmission and nerve conduction.[75]

Safety

B vitamins are generally safe when taken at the recommended dosages and side effects are rare, however high levels of these nutrients can lead to some side effects. High doses, typically significantly exceeding the label recommendation of B vitamin products, may lead to contact dermatitis, gastrointestinal symptoms, photosensitivity, high- blood sugar levels, itching, skin flushing, tingling and neuropathy.[76,77,78,79,80]

Interactions

Anticonvulsants: Long term use of anticonvulsant treatment may lead to lower serum biotin status as it increases biotin catabolism, which leads to reduced biotin status and inhibition of intestinal biotin absorption.[81,82,83] Reduced folate levels have also been observed with long term use of this medication. Beneficial interaction is possible, although medical supervision is required.[84]

Oral contraceptives: may deplete vitamin B2, B5, B6 and folate and vitamin B12.[85,86,87,88,89,90]

Antacids and proton pump inhibitors: reduce the absorption of vitamin B12 and folate.[91] It has been hypothesised that since gastric acidity is required for vitamin B12 absorption, acid suppression may lead to malabsorption and ultimately vitamin B12 deficiency.[92] Beneficial interaction is possible. Separate doses by 2-3 hours.

Antidepressants: Supplementation with folic acid/folate resulted in significantly higher plasma folate, lower Hcy, greater improvements in depressive symptoms and fewer reported side effects in a number of clinical trials and retrospective analyses.[93,94,95,96,97] Therefore, beneficial interaction is possible.

Diabetes medication (metformin): may decrease the level of Vitamin B12 and folate. Beneficial interaction is possible.[98,99,100,101]

Methotrexate: is a folate antagonist. There may be a beneficial interaction however, folate may reduce the efficacy of methotrexate, so medical supervision is advised.[102]

Antibiotics: including streoptomycin, erythromycin and aureomycin may reduce the absorption and/or metabolism of Vitamin B5,[103] vitamin B6, Vitamin B12 and folate.[104] Beneficial interaction is possible, however separating the dose by 2-3 hours is recommended.

Blood pressure lowering medications: studies investigating thiamine status in patients with congestive heart failure taking loop diuretics have consistently shown the prevalence of biochemical thiamine deficiency.[105,106,107] Vitamin B3 can have an additive blood pressure lowering effect with anti-hypertensive drugs, opioids, antipsychotics and phosphodiesterase type 5 inhibitors which may result in hypotension, therefore additional blood pressure monitoring is recommended.[108]

Anticoagulants: high doses of B3 (>2,000 mg/ day) are very rarely associated with small reductions in platelet count and increases prothrombin time, although the effect is so rare and small it's considered clinically insignificant and niacin safe to use with anticoagulants.[109] A regular coagulation panel could be considered when supplementing with vitamin B3.[110]

Sulfasalazine: may decrease the absorption of folic acid.[111]

Warfarin: an open-label study in folate deficient men on warfarin showed that folic acid supplementation significantly affected warfarin clearance but effects on required warfarin dose and international normalised ratio (INR, the coagulation parameter to which treatment is adjusted) were not significant.[112]

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