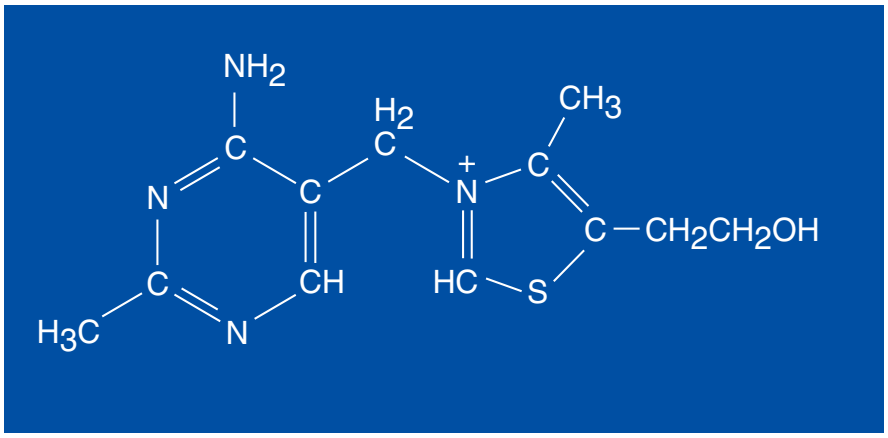

Thiamine

Introduction

Thiamine, also known as vitamin B1, is a water-soluble, B-complex vitamin necessary for metabolism of proteins, carbohydrates, and fats. Thiamine is involved as a cofactor in numerous enzymes, and is essential in every cell for ATP production via the Krebs cycle.

Biochemistry and Pharmacokinetics

Thiamine functions as a coenzyme in more than 24 enzymes, most importantly pyruvate dehydrogenase (for energy production in the Krebs cycle), transketolase (for lipid and glucose metabolism, production of branched chain amino acids, and production and maintenance of myelin sheath), and 2-oxo-glucarate dehydrogenase (for synthesis of acetylcholine, GABA, and glutamate).[1] Thiamine is necessary in the functioning of the hexose monophosphate shunt, an anabolic pathway used proportionately more in adrenal cortex, leukocytes, erythrocytes, and mammary gland tissue. Thiamine is crucial in glucose energy-utilizing pathways, particularly in the central nervous system, which needs a continuous supply of glucose. Thiamine has also been shown to mimic acetylcholine in the brain,[2] which may explain its possible action in Alzheimer's disease and other dementias.[3,4]

The body stores approximately 25-30 mg of thiamine, mainly in skeletal muscle, heart, brain, liver, and kidneys – organs with high metabolic need. In a deficient state, body stores can be depleted in 2-3 weeks.[5] As early as one week after thiamine stores are depleted the blood-brain barrier is disrupted and local cerebral hypoperfusion results, leading to the classic signs of Wernicke's encephalopathy.[6]

Deficiency States and Symptoms

Thiamine deficiency, manifesting as beriberi or Wernicke-Korsakoff psychosis, has been considered to be a problem only in non-developed countries where white rice is a staple of the diet or in advanced alcoholics. However, the work of Lonsdale[7] and others has shown thiamine deficiency occurs in a variety of situations, including a diet high in simple carbohydrates consisting mainly of processed food (sulfites destroy thiamine),[7] complications of alcohol misuse,[8] total parenteral nutrition (TPN),[9] gastrointestinal surgery,[10] severe infection,[11] eating disorders,[12] hyperemesis gravidarium,[13] renal dialysis,[14] cancer (especially if the patient is being treated with chemotherapy),[15] long-term diuretic use,[16] and AIDS.[17] Lonsdale has also reported clinical evidence of increased thiamine need in major depressive disorder, inborn errors of metabolism, hyperactivity, and autonomic dysfunction.[1]

Symptoms of thiamine deficiency are diverse, vary with the degree of severity of the deficiency, and include depression, weakness, dizziness, insomnia, back pain, myalgia, muscular atrophy, palpitations, anorexia, nausea, vomiting, weight loss, hypotension, hypothermia, bradycardia at rest, tachycardia with sinus arrhythmia on exertion,[18] constipation, digestive disturbances, memory loss, peripheral neuropathy, pain sensitivity, dyspnea, and sonophobia.[19] Emotional instability, mood lability, uncooperative behavior, and fearfulness with agitation have also been seen in adolescents with documented thiamine deficiency.[20] Signs of severe thiamine deficiency seen in Wernicke's encephalopathy include ataxia, ophthalmoplegia, nystagmus, and delirium.[8]

Thiamine deficiency, diagnosed by plasma levels, red cell transketolase, or thiamine pyrophosphate percentage effect, has been documented in adolescents eating an average American diet,[20] in 38 percent of a group of non-alcoholic psychiatric patients,[21] 33-55 percent of geriatric populations,[22] and 30-80 percent of alcoholic populations.[23,24] Thiamine is also depleted in those exposed to formaldehyde, and by long-term use of the following prescription drugs: phenytoin, penicillins, cephalosporins, aminoglycosides, tetracycline derivatives, loop diuretics, fluoroquinolones, sulfonamide derivatives, and trimethoprim.[25]

Clinical Indications

Alcoholism

Thiamine deficiency in alcoholism stems from a variety of causes. In addition to low intake, absorption is inhibited and hepatic activation of thiamine coenzymes is decreased.[26] Psychosis resulting from chronic alcohol use is believed to be primarily a result of thiamine deficiency, and appears to be on the rise worldwide.[2]

Wernicke's encephalopathy, the condition leading to sensory, motor, and cognitive deficits and the long-term consequence of Korsakoff's psychosis in alcoholics, occurs primarily as a consequence of thiamine deficiency.[27] Treatment of Wernicke's encephalopathy necessitates intravenous thiamine for at least 3-10 days followed by a high potency B-vitamin complex for as long as improvement continues.[8]

HIV/AIDS

Moderate to severe thiamine deficiency has been observed in up to 23 percent of HIV-positive or AIDS-diagnosed non-alcoholic individuals.[17] In prospective epidemiological studies, thiamine intakes above 7.5 mg (the RDA is 1.5 mg) were associated with increased survival. The highest levels of vitamin B1 and vitamin C intake were associated with significantly decreased progression from HIV to AIDS.[28] Thiamine-deficiency encephalopathy has been seen in HIV/AIDS patients with no alcohol abuse history.[11]

Congestive Heart Failure (CHF)

The etiology of heart failure is complex, but evidence for the role of micronutrients, particularly thiamine, is clear.[29] Thiamine deficiency leads to impaired oxidative metabolism. Subsequently, pyruvate and lactate levels increase, leading to vasodilation and possible metabolic acidosis, retention of water and sodium leading to edema, and biventricular heart failure known as "wet beriberi." Reversal occurs with thiamine repletion. Iatrogenic contributions may include the use of cardiac medications (specifically furosemide and digoxin) that decrease thiamine uptake in myocytes. Low whole blood levels of thiamine are evident in CHF patients who have been treated with loop diuretics.[30]

Thiamine supplementation in patients with CHF has been shown to significantly improve left ventricular ejection fraction and raise blood pressure 10 mm Hg, an indication of reversal of the pathological vasodilation seen in cardiac beriberi.[31]

Pregnancy, Hyperemesis Gravidarum, and Gestational Diabetes

Thiamine deficiency is common in pregnancy; in one study, 25-30 percent of pregnant women had low red-cell transketolase levels

compared to controls.[32] Pregnant women with hyperemesis gravidarum have a greater risk of thiamine deficiency, and may need to be supplemented with high doses of thiamine.[13]

Women with gestational diabetes are even more likely to become thiamine deficient; 50 percent of study populations have been shown to have low transketolase levels.[33] In one study, 19 percent of gestational diabetics on standard prenatal thiamine supplementation were thiamine deficient.[35] A significant correlation exists between maternal thiamine deficiency and macrosomia (abnormally high body weight) in infants; however, an even stronger correlation was seen in macrosomic neonates from gestational diabetic mothers when the infants were born thiamine deficient.[34]

Mood and Cognitive Performance

A controlled, one-year trial with 127 young adults given 15 mg thiamine, along with other B vitamins at dosages 10 times the RDA,[4] found the most significant association to be enhanced cognitive function and improved thiamine status in females.

Another controlled trial of thiamine and mood investigated 80 elderly females on 10 mg thiamine daily for 10 weeks.[35] Compared to baseline assessment and placebo, those on thiamine experienced significant increases in appetite, body weight, energy intake, general well-being, reduced daytime sleep, improved sleep patterns, decreased fatigue, and increased activity levels.

Drug-Nutrient Interactions

Thiamine can be depleted by long-term use of the following prescription drugs: phenytoin, penicillins, cephalosporins, aminoglycosides, tetracycline derivatives, loop diuretics, fluoroquinolones, sulfonamide derivatives, and trimethoprim.[25]

Side Effects and Toxicity

Thiamine toxicity from oral dosage is not presently known.[7]

Dosage

Dosages of thiamine are condition-specific. To treat Wernicke's encephalopathy, parenteral thiamine is necessary.[8] Oral doses of 50 mg thiamine daily have been used in alcoholics without encephalopathy to raise RBC transketolase levels.[36] Research by Cheraskin and Ringsdorf of "recommended optimal nutrient levels" found individuals taking 9 mg thiamine daily had fewer symptoms associated with illness and chronic degenerative disease than their peers.[37,38] The authors also suggest a wider range of supplemental intake (5-15 mg daily) may be necessary for those on diets high in refined carbohydrates. Lonsdale[7] has published case studies indicating 150 mg thiamine in divided daily doses may be needed to treat individuals with thiamine deficiency symptoms resulting from increased individual requirements.

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