Why Biotin Is Important?

Biotin, or Vitamin B7 is a member of the family of B Vitamins, which have an essential role in cellular metabolic processes. Like most vitamins, humans cannot synthesize biotin and are completely dependent on nutritional sources, gut bacteria that synthesize biotin and a recycling pathway in the body. Biotin is readily absorbed from the gastrointestinal tract from the breakdown of proteins that have attached biotin. Free biotin is released from this breakdown process by an enzyme called biotinidase. Biotin is then transported across the gut attached to a specific transporter protein or by passive diffusion if concentrations in the gut are high enough [1]. Biotinidase is also found in various organs of the body as well as the brain where it recycles free biotin.

The role of biotin in healthy metabolism has been illustrated by conditions of biotin deficiency or inherited defects in biotin transport, biotinidase and biotin attachment [1, 2, 3]. Biotin can also reverse the neurological damage in a rare, genetic condition called biotin responsive basal ganglia disease (BBGD), which is caused by a defect in thiamine transport [4, 5]. Nutritional deficiency can result from prolonged intravenous feeding without biotin supplementation, certain infant hypoallergenic nutritional formulations lacking biotin [6], or excessive consumption of raw egg whites. The latter contains a protein called avidin, which binds biotin very tightly, preventing uptake [1, 3]. Biotin-dependent enzymes can also be reduced by certain medications, in particular certain antiepileptic drugs [7]. Biotin was discovered in the early 20th century when a substance from yeast was found to be necessary for the growth of bacteria in a vitamin deficient media. Later, the term ‘egg white injury’ was applied to laboratory animals manifesting skin and nervous system abnormalities when fed a raw egg white diet [8]. In BBGD, infants and children suffer from severe neurological symptoms, including seizures, incoordination, loss of muscle tone and strength and episodes of unresponsiveness [4, 5]. If given quickly enough, these symptoms can be dramatically reversed with oral biotin administration, co-administration of biotin and thiamine or thiamine alone [9]. Approximately, one in 60,000 infants are born with a total or partial deficiency in biotinidase with similar neurological, as well as dermatological, sequela that is also completely corrected with biotin supplementation (range of 10-
20 mg daily). Today, most states have mandated screening at birth for biotinidase deficiency. Lesser degrees of biotin deficiency can cause dermatological manifestations, including dry skin, dermatitis, hair loss, and atrophy of the tongue. Other neurological manifestations of biotin deficiency include depression, fatigue, muscle pains, and hypersensitivity and pain of the skin [10].

What does biotin do?

Like other B vitamins, biotin – also known as Vitamin B7, Vitamin H, coenzyme R - is involved in a variety of biological processes. It functions as a coenzyme to four essential enzymes called carboxylases. Carboxylases transfer carboxyl groups to other organic molecules in various chemical reactions. Biotin is the carrier molecule for the carboxyl group that it transferred. Biotin is attached to the carboxylases through a linkage with lysine (biocytin). When the reaction is completed, free biotin is released from its lysine attachment by biotinidase to participate in further reactions [1,2,3,11].

![Diagram of biotin and CO₂-biotin]

Biotin functions as a prosthetic group. It binds to enzymes by forming an amide link to an amino group of a lysyl residue.

The four carboxylase enzymes that require biotin are (3):

1) pyruvate carboxylase, which converts pyruvate to oxaloacetate. This reaction is part of the citric acid cycle, which converts glucose to carbon dioxide, generating energy through energy rich intermediates that enter
oxidative phosphorylation in the mitochondria. High lactic acid levels result from reduced activity of this enzyme;

2) propionyl-CoA carboxylase, which is involved in the breakdown of branched chain amino acids and odd-chain fatty acids. It catalyzes the conversion of propionyl-CoA to methylmalonyl-CoA;

3) \textit{B}-methylcrotonyl-CoA carboxylase, which participates in the breakdown of leucine;

4) Acetyl-CoA carboxylase, which is involved in the first committed step of fatty acid synthesis in the conversion of acetyl-CoA to malonyl-CoA.

It is the latter reaction that may be most relevant in central nervous system disease. Both acetyl-CoA carboxylase and pyruvate carboxylase are found in high amounts in myelin-producing oligodendrocytes in the central nervous system in rats and may have higher biotin requirements [12]. Fatty acids are building blocks for myelin and these reactions are the rate-limiting for myelin production. Both demyelination and axonal degeneration were pathological features in a biotinidase-deficient mouse model of biotin deficiency [13]. Biotin deficient rats showed impairment in a learning test of avoidance [14].

\textbf{Biotin in Health and Disease}

Given its effect on glucose and lipid metabolism, is biotin potentially a treatment for metabolic abnormalities? In studies involving mice fed a biotin supplemented diet was found to decrease serum triglycerides and lipogenic gene expression in liver and adipose tissues [15]. Other studies also confirm the beneficial effects of biotin on lipid and glucose metabolism [16].

\textbf{Biotin in Multiple Sclerosis}

One potentially intriguing use of biotin is in the treatment of patients with progressive multiple sclerosis, which is believed to involve a combination of inflammation and neurodegeneration. In an open-label study, 23 subjects with primary and secondary progressive forms of multiple sclerosis were treated with doses of biotin ranging from 100 to 300 mg daily from two to 36 months [17].
Outcome measures included visual acuity, visual fields, visual evoked potentials, walking distance, EDSS, the 25 foot timed walk and the choline/creatin ratio.

Improvement in impairment was reported using objective and subjective measures. One patient with progressive visual loss improved on visual field testing up to 16 months. Of 18 patients with significant motor weakness, 16 of 18 patients showed various degrees of improvement (89%) after two to eight months of treatment. Improvement in nine patients was confirmed by a blinded review of videotaped examinations. Five of seven ambulatory patients with walking impairment improved on the 25-foot timed walk scale from 17.6 to 33.8 percent. Examining neurologists also noted improvement in other symptoms, including fatigue, swallowing dysfunction, dysarthria, sensory signs, gait ataxia and urinary dysfunction. Cognition, psychiatric symptoms, oscillopia, coordination, and Uhtoff’s phenomenon. The EDSS improved in 4/23 patients (22%). In one patient, the choline/creatine ratio measured by NMR spectroscopy normalized after nine months, an index of axonal protection. Four patients during the study experienced at least one relapse of their multiple sclerosis. Adverse events were reported in three patients, including transient diarrhea in two patients and a death in one patient from heart failure 36 months after the start of treatment. Another patient who had been on treatment for one year died of pneumopathy a few days after abdominal surgery.

Results in two additional studies have been reported [18]. One 48-week randomized, double-blinded, placebo-controlled study involved 154 subjects with progressive multiple sclerosis. A significant percentage of subjects in the biotin-treated group showed clinical improvement compared to the placebo-controlled group. Another 24-week, randomized, double-blind, placebo-controlled study in 93 subjects with chronic visual loss secondary to optic neuritis did not show significant improvement between the biotin-treated group and placebo on contrast visual acuity.

Proposed Mechanism of Action of Biotin in Multiple Sclerosis

While it is unlikely that patients with multiple sclerosis have any defects in biotin utilization or metabolism, one study did show that patients with multiple sclerosis had lower levels of biotin in cerebrospinal fluid and serum and a reduced
CSF/serum ratio of biotin compared to healthy individuals as well as individuals with other neurological diseases [19]. The authors speculate that the lower biotin levels may be due to an underlying intestinal malabsorption or an unidentified biotin-binding immunoglobulin related to MS pathogenesis.

Mechanisms that may help explain the effects of high dose biotin in the progressive MS trials include its role in the production of fatty acid substrates for the synthesis of myelin in oligodendrocytes as well as its more general role in enhancing cellular energy production [20].

REFERENCES


