In this issue, we look at the therapeutic applications of the active forms of two B Vitamins – Folinic Acid and Methylcobalamin in mental health.

B Active

Use of the water soluble B group vitamins to support nervous system function is a well accepted initial treatment option. Further research into the intricate biochemistry of the human body, has revealed that many of these B vitamins have active forms which demonstrate enhanced activity and utilization over the other well known forms. For example, pyridoxine or vitamin B6 is commonly prescribed in its active form of pyridoxal 5-phosphate and used very successfully in conjunction with other nutrients to treat depression, anxiety, pre-menstrual tension, morning sickness and cardiovascular system support to name but a few.

Recently, more attention has been directed at the active forms of folate and vitamin B12 – folinic acid and methylcobalamin particularly when addressing depression and autism.

Folate

Folic acid occurs naturally as a complex of related substances called folates which are found in foods such as sprouts, beans, eggs, lentils, Brewer's yeast, organ meats and green leafy vegetables [1]. However, food preparation and processing can destroy almost all of the naturally occurring folate, as it is highly sensitive to heat, air and light [2]. Oral folates are generally available in two supplemental forms: folic and folinic acid. Although the most common supplemental form of the folates is folic acid, it only makes up 10% or less of dietary folates. The majority of folates in the diet consist of reduced folates and methyltetrahydrofolates. Although folic acid is generally well absorbed, evidence suggests that reduced folates and methyltetrahydrofolates are absorbed differently [3].

Folinic Acid

Administration of folinic acid bypasses the deconjugation and reduction steps required for folic acid. Folinic acid has been deemed to be a more metabolically active form of folate, which is capable of boosting levels of the coenzyme forms of the vitamin in circumstances where folic acid has little to no effect. It is also suggested that folinic acid is also more readily transported through the blood brain barrier into the central nervous system and has a longer half-life in the body than folic acid [3]. Human absorption kinetic studies of orally administered folinic acid have demonstrated a bioavailability of 92% [4]. Following an oral dose of folinic acid, the majority of folates are metabolized to 5-MTHF directly during absorption in the intestine, bypassing the need for deconjugation and subsequent reduction in the liver [3].

Folinic acid has largely been reserved for the use of methotrexate rescue and as an adjunct to some chemotherapy drugs.

Therapeutic Uses of Folinic Acid

Therapeutically, folic acid can reduce homocysteine levels and the occurrence of neural tube defects, may play a role in cervical dysplasia and protecting against neoplasia in ulcerative colitis. Folic acid deficiency is considered to be one of the most common nutritional deficiencies [3].

Patients with major depressive disorder often demonstrate lower serum and red blood cell folate concentrations. Lower serum folate concentrations have been closely associated with greater severity of depression [3]. Some evidence also suggests that low folate levels can result in a poorer response to selective serotonin reuptake inhibitors (SSRIs) [5]. It has also been reported that the efficacy of conventional antidepressants such as fluoxetine (Prozac) is significantly enhanced by the addition of daily folate [6, 7].

Vitamin B12 (Methylcobalamin)

The Link to Homocysteine

Since the discovery of folate in 1945 and vitamin B12 in 1948, numerous reports have described the neuropsychiatric complications associated with deficiencies in these vitamins. There are similarities and differences observed in folate and vitamin B12 deficiency, which stem largely from their intimate metabolic relationship. The central biochemical reaction that unifies these two vitamins is in the methylation of homocysteine to methionine, which is catalyzed by methionine synthetase. Diminished activity of this enzyme and the consequential rise in homocysteine can lead to severe metabolic consequences as homocysteine is not only toxic to vascular endothelial cells but also to neuronal cells. Elevated blood levels of homocysteine have been associated with several psychiatric and neurodegenerative disorders including depression, schizophrenia, Alzheimer's disease and Parkinson's disease [8].

Low concentrations of 5-hydroxyindole acetic acid (5-HIAA – a serotonin metabolite) which gives an indicatation of systemic serotonin tissue levels, have been reported in folate-deficient patients with various neuropsychiatric illenesses [9], epilepsy[10] and severe depression [11]. In another study of folate deficient patients, low levels of 5-HIAA, homovanillic (HVA – a dopamine metabolite), and 3-methoxy-4-hydroxyphenylglycol (MHPG – a norepinephrine metabolite) were all significantly reduced in a sub-group of depressed patients with high plasma homocysteine levels [12].

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