

B Vitamins for ADHD

Overview:

There is tremendous individual variation in B vitamin status. Some kids might need B₆ more than others.

Background:

There are two important forms of vitamin B₆: pyridoxine - the form given as a supplement and pyridoxal phosphate (PLP) - the metabolically active form which is required for the synthesis of neurotransmitters: serotonin, dopamine, epinephrine, norepinephrine, and gamma-aminobutyric acid (GABA).

Rationale:

Biochemical disturbances in ADHD (serotonin and catecholamine deficiency, glutamate/GABA imbalance, and plasma tryptophan excess) may be related to vitamin B₆ status. Many neurotransmitters are formed or metabolized by PLP-dependent enzymes. Some ADHD patients have dramatically impaired pyridoxine-dependent enzyme activity.

Science:

Tryptophan was measured in the urine of 41 healthy controls, 13 untreated ADHD patients, and 10 ADHD patients treated with Ritalin aged 6-11. ADHD patients had dramatically impaired activity of pyridoxine-dependent enzymes. The imbalance was corrected to some extent in patients on Ritalin.

Dolina, S., Margalit, D., Malitsky, S., & Rabinkov, A. (2014). Attention-deficit hyperactivity disorder (ADHD) as a pyridoxine-dependent condition: Urinary diagnostic biomarkers. *Medical Hypotheses*, 82(1), 111-116.

Blood serotonin measured in 11 hyperactive outpatients and 11 controls aged 3-13. Compared to controls, hyperactive children had significantly lower serotonin in their blood. When hyperactive patients were given pyridoxine supplements, blood serotonin and PLP increased.

Bhagavan, H. N., Coleman, M., & Coursin, D. B. (1975). The Effect of Pyridoxine Hydrochloride on Blood Serotonin and Pyridoxal Phosphate Contents in Hyperactive Children. *Pediatrics*, 55(3), 437.

Pyridoxine might be as effective as or more effective than methylphenidate - even in patients who were previous methylphenidate responders. 6 hyperactive patients aged 8-13 with low blood serotonin levels who previously responded to methylphenidate completed a double blind crossover trial with pyridoxine, methylphenidate, and placebo for 21 weeks total. Teachers and parents rated children as on their best behavior (least hyperactive) when on pyridoxine. Pyridoxine but not methylphenidate elevated blood serotonin levels.

Coleman, M., Steinberg, G., Tippet, J., Bhagavan, H. N., Coursin, D. B., Gross, M., & ... DeVeau, L. (1979). A preliminary study of the effect of pyridoxine administration in a subgroup

of hyperkinetic children: A double-blind crossover comparison with methylphenidate. *Biological Psychiatry*, 14(5), 741-751.

Case study of 3 year old female. Insomnia, irritability, hyperactivity, and temper tantrums developed after isoniazid treatment. Pyridoxine 400 mg/day completely controlled all symptoms. Both isoniazid and pyridoxine therapies were discontinued after 6 months. Behavioral problems returned. Patient described as wild, easily distracted, and disruptive. Pyridoxine therapy started again. Great improvement noted several days later. Dosage of 400 mg/d was needed to successfully control the neuropsychiatric symptoms. During 6-year follow-up, patient remained asymptomatic while taking pyridoxine 300 to 400/mg/day. Any periodic cessation of vitamin therapy or substitution of a placebo led to a rapid return of irritability, hyperactivity, hostility, and aggression which developed within 2 weeks.

Brenner, A., & Wapnir, R. A. (1978). A pyridoxine-dependent behavioral disorder unmasked by isoniazid. *American Journal Of Diseases Of Children* (1960), 132(8), 773-776.

Possible Mechanisms:

B vitamins and methylphenidate may share a common neurochemical mechanism.

Methylphenidate elevates dopamine levels by inhibiting reuptake of dopamine. It binds with the dopamine transporter (DAT) on the presynaptic cell membrane and prevents dopamine from binding there. Thus reabsorption of dopamine is inhibited. B vitamins and their relationships with dopamine may be responsible for their effect on ADHD symptoms. B vitamins competitively bind to the DAT dopamine binding sites → increase in synaptic dopamine concentration → postsynaptic dopamine D2 receptor activated → improved ADHD symptoms
Shaw, I., Rucklidge, J. J., & Hughes, R. N. (2010). A possible biological mechanism for the B vitamins altering behaviour in attention-deficit/hyperactivity disorder. *Pharmaceutical Medicine*, 24(5), 289.