

ADHD PLUS MINUS TREATMENT PLAN

+ ZINC -COPPER

Dr. James Greenblatt, MD

The plan below is part of a guide for practitioners to add elements (+) or remove them (-) from the patient's environment or lifestyle as treatment for ADHD symptoms. Biochemical individuality will determine the most important elements for each patient.

ZINC AND COPPER

Zinc (Zn) plays a role in the production of proteins, enzymes, and neurotransmitters. The dopamine transporter is uniquely zinc-dependent, suggesting a role for zinc in dopaminergic transmission (Pifl et al., 2009; Li et al., 2015). In addition, Zn is necessary for the myelination of nerves and for proper nerve signal transmission involved in learning and memory. Zn also helps the production of melatonin and digestive enzymes. Low Zn can result in learning, sleep, attention, mood, and digestive problems (Gower-Winter et al., 2012).

Zinc in ADHD

Children with ADHD have been shown to have lower levels of Zn than controls (Arnold et al., 2005; Elbaz et al., 2017; Yang et al., 2019; Skalny et al., 2020). The symptoms of ADHD that are associated with low zinc are inattention, hyperactivity, and impulsivity (Viktorinova et al., 2016; Elbaz et al., 2017). El-Bakry et al. (2019) showed zinc to be significantly lower in males with ADHD than females with ADHD, suggesting a sex difference in mineral status.

Copper-Zinc Balance

Copper (Cu) is likewise an important mineral, but daily requirements are much lower than for zinc. Cu and Zn have an inverse relationship: excess Cu depletes Zn in the body and causes Zn deficiency symptoms. Excess Cu can also directly damage the liver, kidneys, and the CNS, as in Wilson's disease (Gaetke et al., 2003). The Cu:Zn ratio has been found to be significantly higher in children with ADHD than in controls (Viktorinova et al., 2016, Skalny et al., 2020).

Even mildly elevated Cu may be involved in free radical production and oxidative damage that results in mitochondrial damage, DNA breakage, and neuronal injury (Desai et al., 2008). Levels of serum Cu/Zn superoxide dismutase (SOD) has been shown to be lower in patients with ADHD, indicating increased oxidative stress (Russo, 2010).

Zinc Supplementation

Several intervention studies demonstrate significant or positively trending results for ADHD symptoms after treatment of 6-12 weeks of oral zinc (Akhondzadeh et al., 2004; Bilici et al., 2004; Zamora et al., 2011; Noorazar et al., 2020).

In the above studies, improvements were noted in inattention, hyperactivity, and socialization scores, and in various rating scales (ie. the Conners global index ADHD rating scale (CGI), and Parent and Teacher Rating Scale scores).

Zinc and Stimulant Medications

Low zinc may also interfere with the function of stimulant medications for ADHD (Lepping et al., 2010). One study showed that zinc-deficient children were less likely to respond to dextroamphetamine treatment (Arnold et al., 1990). Akhondzadeh et al. (2004) demonstrate a larger improvement with zinc and methylphenidate compared to methylphenidate alone. Another study showed a 37% decrease in the optimal dose of methylphenidate with 30mg Zn as an adjunct treatment (Arnold et al., 2011).

Causes of a Cu:Zn imbalance

Lifestyle and physiological factors decrease Zn in the body, since Zn is lost in sweat, in stress, and higher amounts are required in puberty and pregnancy. A patient has a greater risk of Zn deficiency if they exercise frequently, if they are eating a vegan/vegetarian diet, or going through puberty. Copper excess most often results from drinking water, copper pipes, and cookware.

ADHD PLUS MINUS TREATMENT PLAN

+ ZINC -COPPER

Dr. James Greenblatt, MD

The plan below is part of a guide for practitioners to add elements (+) or remove them (-) from the patient's environment or lifestyle as treatment for ADHD symptoms. Biochemical individuality will determine the most important elements for each patient.

TEST

Hair tissues mineral analysis is the test that best detects long-term mineral deficiencies and imbalances. It is important to also assess levels of lead (Pb) in the hair mineral analysis as well, as this heavy metal has strong associations with neurological and physical symptoms.

INDICATIONS

Signs and symptoms indicating mineral analysis:

- Stimulant medication doesn't work or exacerbates
- Child is extremely limited in what they will eat, or has digestive concerns
- Transverse leukonychia (white spots on nails)
- Vegan/vegetarian diet
- Sleeping problems, especially as an infant
- Puberty, stress
- Competitive athlete, frequent exercise

Selective eating behaviours and digestive function are both associated with zinc because digestive enzymes are Zn-dependent, as is the function of taste.

SOURCES

1. Pifl et. al., (2009). *Neuropharmacology*, 56(2), 531-540
2. Li et. al., (2015). *Journal of Biological Chemistry*, 290(52), 31069-31076
3. Gower-Winter, et. al., (2012). *Biofactors*, 38(3), 186-193
4. Arnold et. al., (2005). *Journal of Child & Adolescent Psychopharmacology*, 15(4), 628-636
5. Elbaz et. al., (2017). *Egyptian Journal of Medical Human Genetics*, 18(2), 153-163
6. Yang et. al., (2019). *Biological trace element research*, 187(2), 376-382
7. Skalny et. al., (2020). *Journal of Trace Elements in Medicine and Biology*, 58, 126445
8. Viktorinova et.al., (2016). *Biological trace element research*, 169(1), 1-7
9. El-Bakry et. al., (2019). *Egyptian Journal of Psychiatry*, 40(2), 95
10. Gaetke et. al., (2003). *Toxicology*, 189(1-2), 147-163
11. Desai, et. al., (2008). *The American journal of clinical nutrition*, 88(3), 855S-858S
12. Russo, (2010). *Journal of central nervous system disease*, 2, JCNSD-S4553
13. Akhondzadeh et. al., (2004). *BMC psychiatry*, 4(1), 9
14. Bilici et. al., (2004). *Progress in Neuro-Psychopharmacology and Biological Psychiatry*, 28(1), 181-190
15. Zamora et. al., (2011). *Archivos latinoamericanos de nutricion*, 61(3), 242-246
16. Noorazar et. al.,(2020). *Asian Journal of Psychiatry*, 48, 101868
17. Lepping et. al., (2010). *CNS drugs*, 24(9), 721-728
18. Arnold et. al., (1990). *Int'l journal of Neuroscience*, 50(1-2), 103-107
19. Arnold, et. al., (2011). *J. child and adolescent psychopharmacology*, 21(1), 1-19

TREAT

Zinc picolinate is the most studied and best absorbed form, and has less gastrointestinal discomfort than zinc sulfate (Arnold et. al., 2011).

Dosing

- Age 12+: 30mg bid with meals
- Age 6-11: 15mg bid with meals
- Age 5 and under: zinc supplementation is not advised, unless a strong deficiency is present, in which case investigate causes of zinc deficiency including poor absorption and gastrointestinal disorders.

Retest after 6 months. If symptoms and mineral levels are both corrected, reduce dosage to daily multimineral with 15mg zinc. If levels have normalized but symptoms are not corrected, consider adding a stimulant that may be more effective after normalizing mineral levels. You can expect to see a change in behaviour in up to 3 months of oral zinc treatment.

Safety

Zinc supplementation may force copper out of cells and cause temporary worsening of symptoms, including headache, stomachache, agitation and hyperactivity. If this rare reaction happens, stop zinc for a few days then restart zinc at reduced dose. Increase after three weeks.