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Vitamin D and Depression

Peter Bongiorno ND, LAc

The World Health Organization predicts depression as the second most burdensome disease in the next decade with the greatest burden in North America and the United Kingdom. Currently, major depression accounts for 33.3% of patients in the United States and, at 160 million prescriptions annually, anti-depressants are the most prescribed medication, despite the fact that recent meta-analyses show these as no better to treat mild to moderate depression (the major prescriptive reason) than placebo.

Depression has multi-factorial causes and requires looking into emotional and spiritual issues, diet, and lifestyle factors, as well as choosing appropriate supplemental therapies for individualized care. Vitamin D may help the integrative practitioner treat a critical underlying deficiency. Known best in calcium regulation, Vitamin D is gaining attention for playing a role in a number of diseases including autoimmune conditions, cardiovascular diseases, cancers, and chronic pain. A recent meta-analysis even suggests reductions in all-cause-mortality with Vitamin D supplementation.

Low levels of Vitamin D could be involved in the pathogenesis of depression in several ways. In human beings, the distribution of the Vitamin D receptor seems to occur in high concentration in the hypothalamus, suggesting a role in neuroendocrine function. Moreover, the distribution of target neurons of Vitamin D suggests an influence on levels of nerve growth factor, acetylcholine, serotonin, testosterone, thyroid hormone, and tyrosine hydroxylase messenger RNA. All these have all been implicated in the pathogenesis of depression.

So far, human clinical studies seem to bear out a role of Vitamin D in depression. In the largest Vitamin D study of 1282 older adults, mean levels of 25-hydroxyVitamin D were 14% lower in those with minor and major depression compared with controls. In another small study, 44 healthy participants were randomly assigned to 5 days of treatment with 400 or 800 IU of Vitamin D_3 or placebo during winter months. Compared with placebo, both doses of the vitamin increased positive affect and decreased negative affect. A Norwegian study of 441 overweight people measured serum 25-hydroxyVitamin D levels. Those below 16 ng/mL were shown to be more depressed. These subjects were then given 20,000 IU, 40,000 IU, or placebo once a week. Those given 40,000 IU had a 33% reduction in depression scores, those given 20,000 IU had a 20% reduction, and the placebo group had a 5% decrease. Animal studies suggest that prevention of depression in the adult may even occur by treating pregnant moms, as gestational deficiency seemed to cause depression-like behavior in offspring.

Selected populations may be especially prone to low Vitamin D. These include the elderly who have an increased incidence of low Vitamin D, and patients with seasonal affective disorder who do not respond to light therapy.

Vitamin D Dosage

Since Vitamin D is fat soluble, it is advisable to run lab tests before recommending this vitamin. The test indicative of true Vitamin D status is 25-hydroxy (-OH) Vitamin D, which tests for the intermediate metabolite. Research demonstrates that dosages of 4,000 IU qd in depressed patients tend to improve well-being. This may be a good place to start for depressed patients. My clinical experience suggests that dosages of 6,000 to 8,000 IU qd may be necessary for four months to raise levels, followed by a maintenance dose 1,000 to 2,000 IU qd. Weekly doses of 50,000 IU intramuscular have been used clinically, although no long-term studies have been done with these to date. Studies of patients given long-term average of 14,000 IU qd orally showed no toxicity. As a fat soluble vitamin, oral doses should be taken with foods containing fats for best absorption. Although the normal range is usually between 30 and 70 ng/mL, many clinicians regard the optimal levels to be at least 50 ng/mL.

Vitamin D Toxicity

The exact amount of Vitamin D required to induce hypervitaminosis over a given period of time is unknown although some research recommends cautions at 20,000 IU qd or levels of 100 ng/mL. Recent meta-analyses suggests that at ordinary doses (400 to 800 IU qd), long-term Vitamin D supplementation does not seem to be associated with an overall adverse effect. Vitamin D toxicity may lead to hypercalcemia, kidney issues, and excess bone loss.

Vitamin D Forms and Natural Food Sources

When exposed to UVB rays from sunlight, plants manufacture Vitamin D_2 (ergocalciferol), whereas Vitamin D_3 (cholecalciferol) is synthesized by humans in the skin. There is contrasting information on whether Vitamin D_2 or D_3 is most effective. Pharmacopoeias have regarded these 2 forms as equivalent and interchangeable based on 1930's studies in infant rickets prevention. Using the lab test 25-hydroxy (-OH) Vitamin D the form of D_3 has been revealed to be the more potent form of Vitamin D in all primate species, including humans. An emerging body of evidence suggests D_3's greater ability to raise serum levels, diminished binding of Vitamin D_2 metabolites to Vitamin D binding protein in plasma, and a shorter shelf life of Vitamin D_2. For now, the form of Vitamin D used in major preparations of prescriptions in North America is as Vitamin D_2.

Sources of Vitamin D

Food sources include oily fish, eggs, and butter. The main dietary source of Vitamin D is fish. The inverse correlation between fish consumption and depression has usually been interpreted as an association between omega-3 unsaturated fats and depression. However, if this association does reflect cause and effect, Vitamin D is also a factor to consider. Patients should assure adequate amounts of sunlight to increase levels of Vitamin D. One report specifies about 12 min/day in the sun is equivalent to oral intake of 3000 IU of Vitamin D_3. Patients with low serum levels, as well those at higher risk for melanoma and other skin cancers, should be more cautious and should consider foods and a Vitamin D_3 supplement as a first option.

References available upon request

Peter Bongiorno ND, LAc is a graduate of Bastyr University, where he attained his naturopathic doctorate and acupuncture masters degrees. Before medical school, he was a pre-doctoral fellow at the National Institutes of Health and Yale University, in the field of clinical neuro-endocrinology. Peter is co-medical director of InnerSource Health in New York City and Long Island, and acts as Vice President of the New York Association of Naturopathic Physicians. Peter is a major contributor to the third edition of the Textbook of Natural Medicine and has recently authored the textbook Natural and Conventional Therapies for Depression which is to be published in June of 2010. He can be reached through www.InnerSourceHealth.com.