Does Vitamin D Deficiency Cause Depression?

To the Editor: Depression is the most prevalent mood disorder, affecting over 300 million people worldwide, and is a globally significant public health concern.[1] More than 1 in 20 Americans suffer from depression.[2] It is estimated that by 2020 depression will be the second most common cause of disability after ischemic heart disease.[3] Without an established etiology, a combination of factors may contribute to the development of depression including, but not limited to, genetics, stress, substance abuse, low socioeconomic status, isolation, grief, limited social support, and certain disabilities. Hypovitaminosis can result in many different conditions, some of which have an emotional impact.[4] Vitamin D deficiency is associated with depression in some people.[5]

Vitamin D and Depression. There is no specific mechanism to explain how vitamin D deficiency might yield affective illness. Vitamin D receptors in the brain at the prefrontal cortex, hypothalamus, and substantia nigra play a role in regulating emotions.[6] Vitamin D regulates serotonin levels, and vitamin D deficiency leads to diminishing serotonin concentrations.[7] Low serotonin levels could be an etiology for inducing clinical depression.[8]

Vitamin D is hypothesized to increase the expression of genes encoding tyrosine hydroxylase, which regulates the synthesis of dopamine and norepinephrine.[9,10] A decrease in the brain levels of these monoamine neurotransmitters can result in depression.[8] Vitamin D is also responsible for maintaining the homeostasis of calcium and reactive oxygen species by controlling the expression of genes. With a deficiency, calcium and reactive oxygen species concentrations are increased, thereby augmenting cytokines and inflammatory markers that might impact the immune system and induce stress, which secondarily may cause depression.[11]

A meta-analysis[5] involving 8,815 subjects from 3 prospective observational studies documented that there is an elevated risk of affective illness in individuals with low vitamin D levels. A study[11] of the effect of cigarette smoking on hypovitaminosis D and depression found significantly more depression in smokers compared to nonsmokers. The nicotine in cigarette smoke might interfere with intestinal calcium absorption, leading to reduced serum calcium levels. These decreased concentrations elevate parathyroid hormone and alkaline phosphatase levels, which eventually can result in vitamin D deficiency.[12]

Hypovitaminosis D is also documented in patients with seasonal affective disorder,[13] poststroke depression,[14] and other medical conditions such as diabetes mellitus,[15] spinal cord injury,[16] and chronic renal disease.[17] Among patients hospitalized for an affective illness, depression reportedly is more severe in those with coexistent vitamin D deficiency.[18]

Discussion. Hypovitaminosis D is associated with depression.[11] Vitamin D prescribed as an adjunct to antidepressant pharmacotherapy may diminish depressive symptoms.[19] Assays measuring vitamin D concentrations in patients with depression could have diagnostic and therapeutic implications. Reliance on such laboratory analyses is a clinical decision; for example, such testing might be particularly indicated in patients unresponsive to previous therapies. Suboptimal vitamin D levels mandate supplementation.

Clinicians should stress the importance of vitamin D in the diet and adequate sun exposure, as well as the risks of overexposure. Greater physician and patient awareness of hypovitaminosis is recommended. Vitamin D levels should be monitored during health checkups, especially in patients with long-standing affective symptoms, as such monitoring might help reduce the prevalence of overt depression. Vitamin D supplementation, when indicated, can sometimes be a powerful adjunct pharmacotherapy for patients with depression.

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Shanti Pittampalli, MD[a]
Hema Madhuri Mekala, MD[a]
Satya Upadhyayula, DMD, MS[a]
Steven Lippmann, MD[a]
steven.lippmann@louisville.edu

[a]University of Louisville School of Medicine, Louisville, Kentucky

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