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Vitamin D Deficiency

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Introduction

Vitamin D is a fat-soluble vitamin used by the body for normal bone development and maintenance by increasing the absorption of calcium, magnesium, and phosphate. A circulating level of 25-hydroxyvitamin D greater than 30 ng/mL is required to maintain a healthy level of vitamin D. About 1 billion people worldwide have vitamin D deficiency.[1] Vitamin D deficiency can lead to an array of problems, most notably rickets in children and osteoporosis in adults. The fortification of milk with vitamin D in the 1930s was effective in eradicating rickets in the world. However, vitamin D deficiency is now more prevalent than ever and should be screened in high-risk populations. Many conflicting studies are now showing an association between vitamin D deficiency and cancer, cardiovascular disease, diabetes, autoimmune diseases, and depression.[2]

Etiology

Vitamin D deficiency arises from multiple causes including inadequate dietary intake and inadequate exposure to sunlight. About 50% to 90% of vitamin D is absorbed through the skin via sunlight while the rest comes from the diet. Twenty minutes of sunshine daily with over 40% of skin exposed is required to prevent vitamin D deficiency.[3]. Certain malabsorption syndromes such as celiac disease, short bowel syndrome, gastric bypass, and cystic fibrosis may also lead to vitamin D deficiency. Moreover, medications such as phenobarbital, carbamazepine, dexamethasone, nifedipine, spironolactone, clotrimazole, and rifampin induce hepatic p450 enzymes which speed up the degradation of vitamin D.[4] Lastly, people with chronic liver disease and chronic kidney disease are at high risk for vitamin D deficiency due to the steps of enzymatic hydroxylation by the liver and kidney to activate vitamin D.

Epidemiology

It is important to note that vitamin D deficiency is a major global public health issue. About 1 billion people worldwide have vitamin D deficiency, while 50% of the population has

vitamin D insufficiency.[1] The prevalence of patients with vitamin D deficiency is highest in the elderly, the obese patients, nursing home residents, and hospitalized patients. Prevalence of vitamin D deficiency was 35% higher in obese subjects irrespective of latitude and age.[5] In the United States, about 50% to 60% of nursing home residents and hospitalized patients had vitamin D deficiency. [6][7] Vitamin D deficiency may be related to populations who have higher skin melanin content and who use extensive skin coverage, particularly in Middle Eastern countries. In the United States, 47% of African American infants and 56% of Caucasian infants have vitamin D deficiency, while over 90% of infants in Iran, Turkey, and India have vitamin D deficiency. In the adult population, 35% of adults in the United States are vitamin D deficient whereas over 80% of adults in Pakistan, India, and Bangladesh are Vitamin D deficient. In the United States, 61% of the elderly population is vitamin D deficient whereas 90% in Turkey, 96% in India, 72% in Pakistan, and 67% in Iran were vitamin D deficient.[8]

Pathophysiology

Individuals with darker skin pigmentation have increased amounts of melanin in their skin which decreases the efficacy of vitamin D absorption; this is why African Americans and Hispanics are at greater risk. Once ingested or absorbed through the skin, the liver transforms vitamin D into 25-hydroxyvitamin D which is a necessary precursor to the active form. People with chronic liver disease and cirrhosis may not form the precursor leading to vitamin D deficiency. If transformed, the kidneys are then responsible for transforming 25-hydroxyvitamin D to 1,25-hydroxyvitamin D, which is the active form of Vitamin D in the body. People with kidney disease may not make the active form of vitamin D leading to vitamin D deficiency. Another cause may include malabsorption syndromes such as inflammatory bowel disease, celiac sprue, short bowel syndrome, celiac disease, and cystic fibrosis.

History and Physical

The majority of patients with vitamin D deficiency are asymptomatic; however, some symptoms to watch for are generalized weakness, fatigue, muscle aches, muscle twitching (fasciculations), osteoporosis, osteomalacia, and depression. In children, irritability, lethargy, developmental delay, bone changes, or fractures are important symptoms of vitamin D deficiency.

Evaluation

Measurement of serum 25-hydroxyvitamin D is the test of choice to determine vitamin D deficiency. Levels of 25(OH)D less than 20 ng/mL indicate vitamin D deficiency while levels below 30 ng/mL indicate vitamin D insufficiency. Levels of 25(OH)D greater than 50 ng/mL

show optimal levels. Measurement of serum PTH may help distinguish secondary hyperparathyroidism in certain patients. It is important to screen for vitamin D deficiency in those at high risk, including patients with osteoporosis, malabsorption syndrome, obese individuals, African Americans, Hispanics, and patients with chronic kidney or chronic liver disease.

Treatment / Management

Research shows treatment with Vitamin D3 compared with Vitamin D2 resulted in greater efficacy, thus favoring vitamin D3 as a treatment of choice.[9]. Adults who are vitamin D deficient require 6000 IU/day of vitamin D3 for 8 weeks or 50,000 IU of vitamin D3 once weekly for 8 weeks.[10] When the serum 25(OH)D level exceeds 30 ng/mL, a 2000 IU/day maintenance dose is recommended. Adults who are vitamin D deficient who are at high risk for obesity, taking certain medications, have a malabsorption syndrome, or African American or Hispanic are recommended to take at least 10,000 IU daily. Once serum 25(OH)D level exceeds 30ng/mL, 3000 to 6000 IU/day maintenance dose is recommended. Children who are vitamin D deficient require 2000 IU/day of vitamin D3 or 50,000 IU of vitamin D3 once weekly for 6 weeks. When the serum 25(OH)D level exceeds 30 ng/mL, 1000 IU/day, maintenance treatment is recommended. According to the American Academy of Pediatrics, infants who are breastfed and children who consume less than 1 L of vitamin D-fortified milk will need 400 IU of vitamin D supplementation.

Pertinent Studies and Ongoing Trials

A meta-analysis of 18 randomized controlled trials (RCT) including over 57,000 subjects found that intake of daily doses of vitamin D supplements decreased total mortality rates.[11] In the Women's Health Initiative, calcium and vitamin D supplementation decreased the risk of total cancer, breast cancer, and colorectal cancer while not changing total mortality.[12] One RCT showed that calcium plus vitamin D substantially reduced all cancer risk in postmenopausal women.[13]

Staging

The severity of vitamin D deficiency is divided into mild, moderate, and severe. A level of less than 20 ng/mL of 25-hydroxyvitamin D is considered mildly deficient. A level of less than 10 ng/mL of 25-hydroxyvitamin D is considered moderately deficient. A level of less than 5 ng/mL of 25-hydroxyvitamin D is considered severely deficient.[14]

Pearls and Other Issues

Low vitamin D levels were associated with type 2 diabetes mellitus.[15]

Enhancing Healthcare Team Outcomes

Vitamin D deficiency is often overlooked in outpatient and inpatient settings. According to the U.S. Preventive Services Task Force (USPSTF), universal screening for vitamin D levels is not recommended; however, it is important to note that screening for vitamin D deficiency in asymptomatic high-risk individuals is paramount in preventing future complications. High-risk populations include nursing home residents, supra-elderly women (over age 80), women with osteoporosis, African American/Hispanic individuals, hospitalized patients, patients with chronic kidney disease, chronic liver disease, and patients with malabsorption syndromes.[7]

Questions

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