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Vitamin D and Multiple Sclerosis

A complex gene–environment interaction might have therapeutic implications.

The frequency of publications involving the role of vitamin D in neuropsychiatric disorders seems to be increasing exponentially. For example, recent studies have found low vitamin D levels in populations with dementia (JW Neurol Mar 30 2010) and in those with depression (Psychosom Med Jul 1 2010). Now, authors of a review article focus on converging lines of evidence for connections between multiple sclerosis (MS) and vitamin D, which has anti-inflammatory activity and decreases T-cell proliferation. Separately, other researchers report on an early study of high-dose vitamin D in patients with MS.

As many of us remember, MS is more common in latitudes with less sunlight. Handunnetthi and colleagues reviewed studies that have connected this association to low levels of serum 25-hydroxyvitamin D (25[OH]D) during gestation, early childhood, and adolescence, or during adulthood. The authors also discussed evidence that variation in the *HLA-DRB1* gene may at least partly contribute to MS risk in a gene–environment interaction. Alleles of this gene have been associated with MS in northern Europeans, and its expression is sensitive to 1,25-dihydroxyvitamin D3. These findings suggest that D3 supplementation may help some patients with MS and should be tested in clinical trials.

Burton and colleagues conducted an open, 1-year, randomized, placebo-controlled, early trial of tolerance of high-dose vitamin D3 plus calcium in 49 patients with MS. Patients were matched for age, disease duration, disability level, and MS drug. Vitamin D doses were gradually escalated to 40,000 IU/day by week 23 and were then gradually titrated downward. Calcium doses were 1200 mg/day. With supplementation, serum calcium level (the primary outcome) showed no significant changes; serum 25(OH)D levels rose to a maximum of 413 nmol/L (which, according to the authors, is above the "cited toxic value" of 250 nmol/L). No adverse events occurred. Although this phase I/II study was not designed for efficacy, **recipients of vitamin D plus calcium appeared to have fewer relapses and less T-cell proliferation than controls.**

Comment: Epidemiologic and clinical evidence suggests that vitamin D has a role in MS, and a cogent rationale exists as to why supplementation may be beneficial. We now have class II evidence of the safety of high-dose vitamin D, but evidence of efficacy is weaker. Rigorous studies are required to demonstrate efficacy, and these should include human leukocyte antigen genotyping. In addition, these gene–environment interactions should be examined in patients with depression or dementia. Clinically, it seems time to obtain baseline 25(OH)D levels in many of our patients for discussion of possible supplementation.

— *Jonathan Silver, MD* *Published in* Journal Watch Neurology *July 27, 2010*

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